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KEY TO ABBREVIATIONS

c — correspondence
cr — case record
e — editorial
ma — medicolegal abstract

mdph — Massachusetts Department of Public Health
mms — Massachusetts Medical Society
mp — medical progress
misc — miscellany

mr — meeting report
n — notice
o — obituary
* — original article

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Number 1

LIGATION OF THE INFERIOR VENA CAVA OR ILIAC VEINS*

A Report of Thirty-Six Operations

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WASHINGTON, D. C.

THE first ligations of the inferior vena cava were performed by Kocher in 1883 and Billroth in 1885,¹ these procedures being the results of operative trauma and both being followed by a fatal outcome. The first successful ligation was performed by Bottini.² Two ligations of this type were performed in 1906 and a third in 1910 by Trendelenburg,^{3, 4} all for thrombophlebitis of the pelvic vein with septicemia, 1 patient recovering. Martens⁵ has reported 2 cases of ligation of the vena cava and 9 of the iliac vein for thrombophlebitic pyemia, 7 of the 11 patients surviving. Krotoski,⁶ summarizing the literature on the subject in 1937, collected 48 cases of ligation of the vena cava, performed by twenty-seven operators. Homans⁷ in 1944 reported 14 cases of surgical interruption of the iliac vein for venous occlusive disease of the lower extremities. In 1945, Kidd⁸ stated that successful ligation of the inferior vena cava for traumatic laceration had been accomplished in 9 cases. Shackelford and Whitehill⁹ have recently reported a ligation of the left common iliac vein for thrombophlebitis complicated by pulmonary emboli. Gaston and Folsom¹⁰ report 2 cases of ligation of the vena cava for bilateral thrombophlebitis with multiple pulmonary infarcts. Collins¹¹ performed ligation of the vena cava for pelvic thrombophlebitis in 8 patients with 1 death. Northway and Buxton¹² reported such a procedure in 10 cases — 3 patients having multiple emboli, 4 chronic edema of the legs with ulcerations, 2 swollen and painful legs without ulcers and 1 epigastric pain associated with phlebothrombosis. No deaths occurred in this series. Buxton and Collier¹³ reported 7 cases of ligation of the vena cava for bilateral disease of the leg vein and 1 of the iliac vein for unilateral disease. Kern and Berman¹⁴ and O'Neil¹⁵ have also added case reports of ligations of the vena cava.

Thus it may be seen that ligations of the great veins of the pelvis and the inferior vena cava, although not new procedures, are relatively infre-

quent in clinical application. In recent years, since such great emphasis has been placed on the prevention and treatment of pulmonary embolism, these procedures have become of mounting interest to the clinician and surgeon. Whether medical or surgical therapy will prove to be the more satisfactory solution for the problem probably depends on information to be gleaned from several more years of experience in the many centers interested. Meanwhile, it is imperative that attempts be made to obtain a critical analysis of the two modes of management, their criteria for diagnosis, the indications for whichever therapeutic methods are used by each school, the methods by which these measures are accomplished and the ultimate end-results. It was the aim of the investigation herein presented to provide the conclusions arrived at from the study of 36 cases of ligation of the iliac veins or the inferior vena cava operated on at the Gallinger Municipal Hospital.

The evaluation of any therapeutic approach to the problem of phlebothrombosis must of necessity await the clarification of the diagnosis of its presence. It has been suggested in a previous article¹⁶ that the clinical syndrome of edema, color changes, extensive tenderness, elevated white-cell count and red-cell sedimentation rate and local and systemic fever does not represent an early lesion of bland thrombosis, but rather an advanced state of the disease or a complicating thrombophlebitis. Operative findings in patients of this type demonstrate that the clot encountered in this phase is usually in a varying stage of fixation to the vein wall and has accordingly been rendered relatively innocuous. Phlebothrombosis resembles no other disease so closely as it does cancer in that the most significant phase of the disease occurs during the period when the diagnosis is the most obscure. In the same article, the clinical unreliability of the highly revered Homans's test was discussed and another method of examination was presented. While the aforementioned criteria for diagnosis continue to per-

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vade the literature, it will be impossible to make a just appraisal of any therapeutic measures

The boundary zone between pure thrombophlebitis with relatively infrequent embolization and phlebothrombosis with its high risk of serious infarction is so broad and yet so vague that even surgical exposure of the clot is sometimes none too satisfactory in settling the issue. This handicap on the surgeon must rest still more heavily on the clinician who deliberately denies himself the certain knowledge of the nature of the disease under treatment. The fallibilities of phlebography were remarked on in the previous publication,¹⁶ and it is notable that this method of examination has suffered a sharp decline in popularity, even among some of its former advocates.¹⁷

SURGERY AGAINST ANTICOAGULANTS

Although it is not the primary intention of this article to discuss the relative merits of anticoagulants and surgical prevention and therapy of pulmonary emboli from peripheral phlebothrombosis, it may be proper to summarize our present attitude toward these two general methods.

In the first place, the anticoagulants, as represented by heparin and dicumarol, possess a threat of serious hemorrhage. We have witnessed at least 2 deaths that were due to their administration. One might well hesitate to increase deliberately a bleeding tendency in a patient whose lung is already oozing from an infarct or in a pregnant woman who has developed a venous thrombosis. Second, there seems to be good reason to believe that these drugs do not have the ability to affect the clots already formed and that their mode of action can only be on propagation of the existing clot. We have become familiar with the treachery of phlebothrombosis. How can one be assured, having made this diagnosis, that the process will not carry the threat of embolus even if halted exactly at the recognized level in the vein? The danger of the existing thrombus, whether great or small, remains for a period while the physician waits for the clot to adhere to the vein wall. Third, the decision concerning when therapy with dicumarol may be safely discontinued cannot be made on any criteria yet established. It is often necessary to reinstitute its use, and the decision for this appears to depend on the clinical signs of extension of the process, a source of danger in itself. Homans⁷ believes that it is impossible to determine by clinical examination whether the process has ceased to extend or is actually extending farther up the vein. Fourth, in contrast, the procedure of proximal venous ligation appears to be more certain. It has been repeatedly demonstrated by various observers to be a safe measure, and allows a prompt return to normal existence in the majority of cases, whereas the use of anticoagulants entails the loss of much time and expense and requires the most diligent care during therapy.

Lastly, the greatest objection to surgical management is apparently residual edema following ligation. In regard to this symptom following ligation of the iliac vein and vena cava, another section of this paper will cover its incidence and etiology.

INDICATIONS FOR LIGATION OF THE INFERIOR VENA CAVA

Fully realizing the inevitable state of flux in medical opinion concerning the entire problem of phlebothrombosis, and especially the management of both the local disease and pulmonary emboli, we have attempted to devise a working outline of the criteria on which the decision for ligation of the vena cava may be based. From our own experience, we have tentatively accepted the following indications: thrombophlebitis of the pelvic veins with pulmonary emboli, pulmonary embolus associated with prostatic tenderness of recent, or presumably recent, origin, especially with demonstration of deep tenderness along the anterolateral region of the rectum, reasonably conclusive evidence of pulmonary infarcts the source of which remains obscure despite diligent search, and venous occlusion of the lower extremities that would otherwise be treated by interruption of the femoral vein alone. The conditions governing the last are as follows: cellulitis or lymphangitis of the upper thigh, infections of the groin or the finding of enlarged and tender inguinal or femoral-triangle lymph nodes, recurrent emboli following bilateral ligation of the femoral veins, femoral phlebothrombosis with tense edema extending above the knee, the operative finding of adherent clot on exposure of the femoral vein, and acute thrombophlebitis extending into the upper thigh clinically, with the presence of pulmonary embolism.

In the prevention and therapy of pulmonary embolism, ligation of the inferior vena cava is related to interruption of the femoral vein not as a substitute but rather as a complement. The medical literature is replete with sizable case series proving that femoral ligations are safe, simple and responsible for a significant decline in the mortality from pulmonary embolism. There remain, however, certain conditions under which low ligations do not suffice and higher ligations than those of the femoral veins seem the procedures of choice. Thrombophlebitis of the pelvic veins with pulmonary emboli cannot be properly handled with any surgical intervention less radical than ligation of the vena cava. Krotoski⁸ prefers to ligate both iliac and ovarian veins under these circumstances, and ligates the inferior vena cava only if the process has advanced far up the iliac veins. This he accomplishes by celiotomy if a one-stage procedure is practicable or by a two-stage extraperitoneal approach if the condition of the patient is extremely poor. It is difficult to understand why the vena cava should not be ligated primarily rather than both

iliac veins Also, it is open to question whether ligation of the ovarian veins is necessary, especially since this procedure adds so much to the operation in comparison to the one-stage interruption of the vena cava No method completely blocks possible transit of emboli from the distal veins, but each method employed merely severs direct communication with the great veins, rendering this mode of transit so tortuous that advance becomes unlikely Ligation of the femoral veins for peripheral phlebotrombosis is based on this principle, and its effectiveness is beyond question We have considered ligation of the vena cava alone as adequate and simple, and the results in our few cases seem to support this contention Among those advocating interruption of the iliac vein and vena cava for embolizing pelvic thrombophlebitis are Bondy, Schottmueller and Beuttner (cited by Ochsner and DeBaKey¹⁸), Huggins,¹⁹ and Martens,⁵ who reported such a procedure in 11 cases, with 7 survivals, and Collins, Jones and Nelson,¹¹ who performed ligation of the vena cava, with 1 death in 8 cases

In a study of 189 fatal cases of pulmonary embolus, Henderson²⁰ found that prostatic-plexus thrombi were at fault in 18 cases (10 per cent) Although the diagnosis of prostatic-plexus thrombophlebitis is difficult to arrive at with certainty, it may be suspected in a patient exhibiting emboli, with an enlarged and tender gland and with tenderness and possibly induration extending along the anterolateral aspect of the rectum, especially developing as a recent finding in a patient already under observation in whom no other source of emboli can be detected Such criteria prevailing, ligation of the vena cava offers the obvious solution

In the series mentioned above, Henderson also found that 86 per cent of all emboli arose in tributaries of the inferior vena cava When there is reasonably conclusive evidence of pulmonary infarction, the source of which is obscure, ligation of the vena cava may be the procedure of selection rather than bilateral interruption of the femoral veins especially in patients whose occupation or social status makes persistent edema particularly undesirable Ligation of the vena cava is appreciably more inclusive in action Rössle²¹ found that in 10 per cent of his cases obscure emboli arose from the veins of the pelvis Bauer²² found that in 10 per cent of cases femoroiliac thrombophlebitis began in the deep pelvic veins Frykholm²³ states that in 16 per cent of his cases of thrombi they occurred in the iliac and pelvic veins

Not infrequently certain adverse circumstances prevail that contraindicate ligation of the femoral vein that would otherwise be performed In the presence of cellulitis or lymphangitis of the upper thigh or infections of the groin or the finding of enlarged and tender inguinal or femoral-triangle lymph nodes, often signifying latent regional infection, operations in this area result in a high incidence of

wound infection, sometimes of grave import When we have compromised with this judgment, acute thrombophlebitis has occasionally supervened on the ligated side, probably precipitated by manipulation of the femoral vein in a potentially septic field

In the earlier days of exploration of the femoral vein we lacked sufficient clinical experience to predict the operative findings from the results of clinical examination As these findings were more closely correlated, it became evident that tense edema extending above the knee does not occur from a simple phlebotrombosis confined below the inguinal ligament, and that when this type of edema does occur, the clot is too closely adherent to the wall of the femoral vein to permit effective and safe thrombectomy When these findings are encountered, and if a classical thrombophlebitis can be excluded, ligation of the vena cava is performed as a primary procedure It is worthy of emphasis that this clinical picture represents gross neglect, and its occurrence in a hospitalized patient is indefensible

On occasion, following bilateral interruption of the femoral veins, the embolic phenomenon continues and the problem of further management arises Under these circumstances, it is apparent that the true source of the emboli has been misjudged This source may be the profunda femoris vein on either or both sides if the superficial femoral veins have been ligated, or it may be the veins of the pelvic viscera The issue may be so clouded that accurate detection is impossible Re-entry of the incisions for higher ligation of the common femoral veins will result in edema of major and permanent degree Ligation of the vena cava provides the most satisfactory solution

Despite careful preoperative examination, there are times when the operator is taken aback by the operative discovery of adherent femoral clot, even though the bedside examination has revealed almost negligible clinical data In such a contingency a higher ligation is desirable, preferably without interference with the femoral vessels

When acute thrombophlebitis of the lower extremity, complicated by embolization, has invaded the upper thigh clinically, there is no surgical alternative to a high ligation

ILIAC-VEIN VERSUS VENA-CAVA LIGATION

During the earlier stages of our studies, we were inclined toward ligation of the iliac vein in the therapy of apparent unilateral disease not manageable by the femoral approach Homans,⁷ however, has since drawn attention to the likelihood of emboli from the apparently normal contralateral extremity Among others emphasizing the frequently bilateral nature of the disease are Frykholm,²³ Neumann,²⁴ Rössle²¹ and Gaston and Folsom¹⁰ It thus seemed that the rationale of iliac ligation was questionable, especially if combined with a femoral ligation on the

opposite side. Ligation of the vena cava is comparable to ligation of either iliac vein, requiring no more anesthesia, exposure, technical skill or time, indeed, it probably requires less of each of these factors than does ligation of the left iliac vein, which is short and lies under the aorta. For these reasons, we have entirely abandoned the iliac approach during the past year.

OPERATIVE PROCEDURE

Having used various types of incision in the exposure of these great veins, we have concluded that the following method is the simplest and most satisfactory one. It possesses the basic advantages of the McBurney incision for appendectomy, with no incidence of hernia, wound infection or denervation of the abdominal wall.

The incision, which is usually 9 to 10 cm in length, is placed 2 to 4 cm medial to the anterosuperior iliac spine on the right and parallel to the fibers of the external abdominal oblique muscle and fascia. This structure is divided in the line of its fibers, with exposure of the underlying internal oblique and transversalis muscles, which are spread widely to expose the peritoneum. This is swept medially, separating easily from the lateral and posterior abdominal walls and carrying with it the ureter and internal gonadal vessels. The inferior vena cava can be easily visualized. By blunt dissection it is carefully separated from the aorta on the left and the bodies of the lumbar vertebrae posteriorly. It is during this mobilization that extreme care must be taken to avoid tearing the lumbar veins, which enter the posterolateral aspect of the vena cava at intervals of 1 to 3 cm. Avulsion of one of these branches results in hemorrhage of the most trying nature. Following complete mobilization of the vein, it is under-run with a ligature carrier and fastened snugly with a nonabsorbable tie. The abdominal wall is closed in layers with interrupted nonabsorbable sutures.

Since the entire procedure is usually completed in ten to fifteen minutes, we have favored spinal anesthesia, utilizing procaine in doses of 40 to 50 mg. This has invariably proved adequate for the operation.

Complaints referable to the operative wound have been notably few and mild, as evidenced by an average of only 1.2 injections of opiate per patient during the postoperative period. There has been no case of ileus, as would be expected in view of the extraperitoneal approach. Any of these patients whose general condition permits can promptly become ambulatory.

There has been no example of shock developing during the procedure, with the exception of a patient who expired at the termination of the closure. Her death, which is discussed in a later section, is believed to have been due to another pulmonary embolus launched before the vena cava was ex-

posed. The amount of blood lost during the entire procedure, provided that the vena cava is carefully handled, does not exceed that lost during a simple appendectomy. In fact, an appendectomy through a McBurney incision seems to be an entirely comparable procedure as regards operative trauma. The mortality attending the procedure is, as Northway and Buxton¹² express it, the result of the disease rather than of the operation itself. O'Neil¹³ and Homans⁷ have suggested that spinal anesthesia, although preferable from the surgeon's viewpoint, may be hazardous owing to the flexed position assumed during the injection, and believe that general anesthesia may present less objection in this respect. It is also possible that the sympathetic paralysis attending spinal anesthesia may predispose to embolization by sudden relaxation of venous and arterial tone in the extremities. The relaxation of the abdominal muscles obtained by spinal anesthesia, however, is highly desirable. We used intercostal procaine block in only 1 patient (Case 9).

Postoperative edema. Collateral venous return following ligation of the inferior vena cava is much more adequate than one would suppose. O'Neil¹³ has divided the collateral pathways into three groups. In the superficial group are the superficial iliac circumflex and superficial epigastric veins connecting the saphenous system with the veins of the abdominal wall and superficial thoracic veins. In the deep group, the deep iliac circumflex, inferior epigastric and lumbar veins connect the external iliac to the internal mammary and ascending lumbar veins. The ascending lumbar trunks begin on either side of the sacral promontory and communicate with the sacral, common iliac, hypogastric and ilio-lumbar veins. As they ascend, they connect with the lumbar veins, the inferior vena cava and the right renal vein. The right lumbar trunk becomes the azygos vein, and the left the hemiazygos vein. To these groups may be added the vena cava-portal vein communications, particularly the retroperitoneal veins of Retzius, the para-umbilical plexus of Sappey and the superior-middle hemorrhoidal venous anastomosis. In light of these extensive side circuits it is readily seen that the collateral circulation after ligation is potentially enormous. O'Neil states that the edema of the legs following ligation of the vena cava is less than that following ligation of the femoral veins. Gaston and Folsom¹⁰ observed only minimal edema of one leg in 1 of their 2 cases. Kidd,⁸ in his report of 9 cases, found no case of persistent edema. Buxton and Collier¹³ found less edema after ligation of the vena cava in 7 cases than after the usual femoral-vein procedure. The patient reported by Kern and Ber-man¹⁴ had no edema up to five months after operation. Collins, Jones and Nelson¹¹ state that the venous pressure returns to normal in a short time after ligation. Whittenberger and Huggins¹⁵ regard edema as unlikely when the vena cava is ligated.

below the renal veins. Pleasants²⁶ found that sudden occlusion of the lower vena cava failed to produce edema unless the iliac veins were also blocked. Northway and Buxton,¹² however, estimate twelve months as the average time required before venous pressure returns to normal and found that all their 10 patients had mild, but no severe, edema. Two required ligations of varicose veins, and 1 a ligation of distended thoracoepigastric veins after ligation of the vena cava. Homans,⁷ recommending ligation of the vena cava if the thrombosis is bilateral and extends to the inguinal ligaments, states his belief that the venous return is poorer than that following iliac interruption because of the loss of the transpelvic venous shunt. Our own findings can be summarized by stating that whenever edema has followed ligation of the vena cava or iliac veins, there has been unequivocal evidence of either persistence or recurrence of the disease process.

DISCUSSION OF CASES

In this series are included thirty-six ligations of the inferior vena cava or iliac veins, — 21 of the former and 15 of the latter, most of the latter having been performed during the early studies. These procedures were done on a total of 35 patients, there being 1 patient who was subjected to ligation both of the left common iliac vein and of the vena cava. During the past year, for reasons previously outlined, we have abandoned the iliac approach. Under our present tentative indications, all these 15 patients would have been subjected to ligation of the vena cava.

The conditions necessitating these operations were as follows: recurrent emboli following bilateral interruption of the femoral veins (2 cases, 1 death), thrombophlebitis of the pelvic veins, with infarctions (2 cases, 1 death), pulmonary emboli associated with venous clot fixed to the wall of the femoral vein and extending into the iliac vein (17 cases, 9 deaths), venous clot, adherent to the femoral vein and extending into the iliac vein, without emboli (11 cases, 1 death), phlebitis of the prostatic veins, with emboli (1 case, patient living), pulmonary emboli associated with venous occlusion of the lower extremities, usually treated by femoral interruption, contraindicated by disease in the groin (2 cases, 1 death).

The following are brief abstracts of the cases in which death occurred during the postoperative period.

CASE 1 (C10449) A 46-year-old Negress was admitted with and treated for bilateral ovarian abscesses. She pursued a downhill course and developed pelvic thrombophlebitis with multiple pulmonary infarcts. Since her condition was critical, the vena cava was ligated under procaine spinal anesthesia. Sudden shock occurred just as the vein was exposed, the right internal iliac vein clotted, and the patient died as skin closure was being performed, 8 minutes after the operation had been begun. Permission for autopsy was refused. It is believed that the patient had embolus in the operating room.

CASE 2 (C6869) A 51-year-old Negress was admitted in congestive failure due to hypertensive heart disease. She developed phlebotrombosis of the femoroiliac vein with multiple infarcts. The vena cava was ligated 15 days after admission, but the patient died 10 days later. Autopsy showed multiple infarcts, cardiac dilatation and thrombosis of the right iliac vein and lower vena cava.

CASE 3 (C465) A 63-year-old Negress was admitted with hypertensive heart disease. She developed left phlebotrombosis and multiple infarcts. The left femoral and left iliac veins each contained an adherent clot. The vena cava was ligated, but death occurred 9 days later. The autopsy findings were the same as those in the previous case, together with a dissecting aneurysm of the aorta and bacterial endocarditis.

CASE 4 (B99304) A 63-year-old man was admitted with suspected pulmonary infarct or pneumonia. He had an infected toe, enlarged femoral and inguinal lymph nodes and a +++ edema of the right leg and foot. The vena cava was ligated on the day of admission, but the patient died 7 days later. Permission for autopsy was refused.

CASE 5 (B96267) A 72-year-old woman was admitted 1 month after mastectomy for carcinoma of the breast. Swelling of the right leg had developed insidiously at home. There was a +++ edema of the entire right lower extremity. The vena cava was ligated, but the patient died 9 days later. Autopsy revealed thrombosis of the right iliofemoral vein, pulmonary edema and bronchopneumonia.

CASE 6 (B93969) A 67-year-old Negro was admitted with multiple infarcts following amputation of a leg for arteriosclerotic gangrene despite prophylactic ligation of the femoral veins. The vena cava was ligated, but the patient died the next day. Permission for autopsy was refused.

CASE 7 (B94818) A 53-year-old Negro was admitted with hypertensive heart disease and pulmonary infarct. The left femoral vein contained an adherent clot. The left iliac vein was ligated. The infarcts continued, and the vena cava was ligated 4 days later, but death occurred 8 days later. No autopsy was performed.

CASE 8 (B94008) A 54-year-old Negress was admitted with diabetes, infarct and minimal leg signs. Each femoral vein contained an adherent clot. The vena cava was ligated, but the patient died 28 days later after a septic course. No autopsy was performed.

CASE 9 (C17519) A 67-year-old Negress, while under medical investigation for probable carcinoma of the colon, developed insidious edema of the left leg. There was a +++ edema, sudden syncope, cyanosis, dyspnea and semistupor. The vena cava was ligated under intercostal block, but the patient died 3 days later. Permission for autopsy was refused.

CASE 10 (B87828) A 40-year-old Negress was admitted with multiple pulmonary infarcts and thrombophlebitis of the right femoroiliac vein. The right common iliac vein was ligated, but death occurred 20 days later. Autopsy showed the above, as well as thrombosis of the cerebral artery.

CASE 11 (B94942) A 24-year-old Negress was admitted with far advanced bilateral pulmonary tuberculosis, Pott's disease, spinal fusion, a draining sinus over the site of fusion possible pulmonary embolus, and phlebotrombosis of the right femoral and iliac veins. The common iliac vein was ligated. The patient died of tuberculosis 14 months later. No autopsy was performed.

CASE 12 (C6161) A 54-year-old Negress was admitted with thrombophlebitis of the left femoroiliac vein and multiple infarcts. The left common iliac vein was ligated, but the patient died 6 days later. Autopsy revealed thrombophlebitis of the common iliac vein and multiple pulmonary infarcts.

CASE 13 (B94968) A 59-year-old man admitted with hypertensive heart disease developed thrombophlebitis of the right femoroiliac vein, possible multiple infarcts and possible bronchopneumonia. The femoral and iliac veins were thrombosed. The iliac vein was ligated, but the patient died 8 days later. Permission for autopsy was refused.

It is manifestly impossible to evaluate the degree, if any, to which surgery contributed to the death of any of these patients. Their preoperative condi-

tion, as in most of those surviving, varied from extremely poor to critical, most of them having serious cardiac or pulmonary lesions or combinations of the two. One is perched on the horns of a dilemma

The gamble is usually lost in patients as critically ill as those in the cases summarized above. The gloomy picture is considerably brightened, however, when one witnesses the dramatic improvement made by

TABLE 1 *Data on 22 Patients Surviving Iliac-Vein or Vena-Cava Ligation*

CASE No	HOSPITAL No	SEX	AGE yr	RACE	INFARCTS	PREOPERATIVE EDEMA	LIGATION	POST OPERATIVE EDEMA	REMARKS
14	C15614	M	48	W	Multiple	+	(bilateral) Vena caval	0	Patient with hypertensive heart disease developed multiple infarcts and his condition became critical. There were no leg signs, but there were acute prostatic swelling and tenderness and induration of anterolateral area of rectum.
15	C13401	M	61	N	One	+++	(right) Right iliac	+	(right) Patient had insidious swelling of right leg for 2 wk and chest pain and hemoptysis for 6 hr before entry. Right common iliac vein was thrombosed.
16	C12902	F	48	N	None	++	(bilateral) Vena caval	++	(bilateral) Patient had insidious bilateral swelling of legs 5 wk after combined resection of rectum. The leg signs were positive and the iliac veins thrombosed.
17	C9704	M	52	W	None	++++	(right) Vena caval	0	Patient had insidious swelling of right leg for 3 wk. Right iliac vein was plugged. Patient readmitted for right thrombophlebitis.
18	C8425	F	66	W	One	+++	(right) Vena caval	0	Patient had had hip nailing 4 mo previously, with nonunion. Following a massive, nearly fatal embolus right leg was swollen.
19	C8234	F	37	N	One	++	(left) Vena caval	+	(left) Patient had a massive embolus following an operation for a fibroid uterus and an ovarian abscess. There was swelling of the left calf and the left femoral vein was plugged.
20	C7296	F	58	W	None	++++	(right) Vena caval	0	Patient had insidious swelling of right leg and thigh during preparation for a gastrectomy. The right iliac vein was thrombosed. Cava later resected.
21	B98021	M	17	N	Questionable	++	(left) Vena caval	0	Patient admitted with questionable pneumonia or infarct. There was acute swelling of the left foot and calf and the left femoral and iliac veins were thrombosed.
22	B93383	M	63	N	Multiple	+++	(left) Vena caval	+	(left) Patient had cellulitis of left leg and thigh with repeated infarcts.
23	B93511	F	44	N	Multiple	0	Vena caval	0	The infarcts accompanied a salpingitis and the patient's condition was critical preoperatively.
24	C11665	M	60	N	None	+++	(right) Vena caval	0	(2 mo) Patient had insidious edema of right leg and thigh 11 days after gastrectomy.
25	C20025	F	42	W	None	0	Vena caval	0	(3 wk) Lumbar sympathectomy was performed for thrombosis of right femoral artery. The right iliac vein was also thrombosed, and the cava was ligated at the same operation.
26	B88180	F	40	N	None	++	(left) Left iliac	+	(left) Patient had thrombophlebitis of left femoral and iliac veins.
27	B90940	M	30	W	None	+++	(right) Right iliac	++	(right) Patient had recurrent femoral phlebitis with chronic edema.
28	B92500	F	26	N	One	+++	(left) Left iliac	++	(left) Patient had postabortal thrombophlebitis of left femoral and iliac veins.
29	B95416	F	68	W	None	+++	(left) Left iliac	0	Left femoroiliac phlebothrombosis developed following the nailing of a fracture of the neck of the left femur.
30	C5252	F	71	C	One	++	(left) Left iliac	0	Patient had insidious swelling of left leg following fracture of the right tibia. There was an embolus after bilateral femoral ligation.
31	B87907	F	44	C	Two	++++	(right) Right iliac	0	Patient had right femoroiliac phlebothrombosis. A left femoral ligation was also performed.
32	B85462	F	66	W	One	+++	(left) Left iliac	0	A left phlebothrombosis during the course of a meningococcal meningitis.
33	B85427	F	69	W	Multiple	+++	(right) Left iliac	++	(right) Patient had a phlebothrombosis of the right leg. The left femoral vein was filled with an adherent clot. A right femoral ligation was also performed.
34	B81965	F	36	W	None	+++	(right) Right iliac	0	An insidious swelling of the right leg followed a thoracic empyema. The right femoral vein was filled with adherent clot.
35	B90320	F	71	W	None	+++	(right) Right iliac	+	(left) An intertrochanteric fracture of the left femur was followed by insidious swelling of the right leg. The right femoral vein was filled with adherent clot. Right and left femoral ligations were also performed.

when he witnesses the sapping of a patient's cardiac and pulmonary reserve from repeated infarctions not amenable to interruption of the femoral vein

other patients who appear as seriously ill. The essential data accumulated on those who survived are presented in Table 1.

SUMMARY

The history of operative interruption of the inferior vena is reviewed

A tentative list of the criteria for ligation of the vena cava is presented and discussed

The reasons for the recent abandonment of the iliac approach are enumerated

The operative technic of ligation of the vena cava is described, and the incidence and etiology of post-operative edema of the extremities are discussed

Abstracts of the case histories of the 13 patients who died following operation and the essential data on the 22 who survived are presented

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NEUROPSYCHIATRY IN THE EUROPEAN THEATER OF OPERATIONS

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THE best way to present this subject is to do it chronologically, discussing various topics just as they developed in the theater Neuropsychiatric services in the European theater were at all times a part of the general medical services For example, in the Division of Professional Services of the Office of the Chief Surgeon, the senior consultant of neuropsychiatry functioned under the chief consultant in medicine Also, in all hospitals the Neuropsychiatry Section was part of the division of the medical service The term "neuropsychiatry" was maintained in keeping with the practice of not separating neurology and psychiatry except for those aspects of neurology that fell within the neurosurgical services

The year 1942 was a ground-laying period in which the foreign theater had comparatively few troops, most of whom were in North Ireland By the end of the year six general hospitals were in operation and all psychiatric services were centered in these hospitals None of these hospitals, however, had wards that were specifically designed for neuropsychiatry Accordingly, plans were drawn so that one medical ward in each general hospital would be converted into a ward for neuropsychiatric patients This plan was adopted for all the general

hospitals that were being built in England for the United States Army The policy of maintaining inpatient, outpatient, rehabilitation and consultation neuropsychiatric services in all station and general hospitals was adopted quite early As the number of general hospitals increased, personnel problems, especially so far as neuropsychiatrists were concerned, developed here and there, and at times the Neuropsychiatric Section was headed by a medical officer who had had little experience in psychiatry This was corrected as soon as possible, and for the most part the services in general and station hospitals were adequately handled

To keep neuropsychiatry intimately related to and part of general medicine was considered extremely important This was in keeping with the definite trend in civilian as well as military medical practice Steps to establish entirely separate hospital units for neuropsychiatry were taken with reluctance and caution, regardless of the experience in the last war and the experience of the British in this war It appeared to be a backward step, but since the American general-hospital installations had only improvised facilities at the time for psychotic patients, it was evident that special provision had to be made Future developments revealed that for the nonpsychotic patient there were many advantages in a separate mental-rehabilita-

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tion unit. In a neurosis or mental-rehabilitation hospital where the patient did not come in contact with physically sick or wounded soldiers the atmosphere of recovery and return to duty could be created and carried on from admission until final disposition. Although the general and station hospitals carried out the same technics of treatment and rehabilitation, the total atmosphere could never be captured. Few of the general hospitals approached the return-to-duty rate of the special neuropsychiatric hospitals, and the latter usually received only the patients whom the general hospitals had been unable to return to duty. Fortunately, the special neuropsychiatric hospitals were large enough to include medical, surgical, x-ray, laboratory and dental services that were at least equal to those found in many other hospitals.

Before the arrival of the senior consultant in neuropsychiatry, steps had been taken to procure a British mental hospital at Exeter, with the object of having a holding place for psychotic patients. This hospital was opened for patients on January 23, 1943. The 36th Station hospital, a special neuropsychiatric unit under the command of Colonel Ernest H. Parsons, arrived just in time to start this function. This was a 250-bed unit, and the installation had room for 350 patients.

Within a month a special rehabilitation section, called the Training Company, was established. It was organized on a strictly military basis, with a captain from the Air Corps, who was a patient, as commanding officer. The wards were turned into barracks and the entire program throughout the day was on a military basis. The daily schedule included reveille, setting-up exercises, drill, military training, athletics and assignment of work details. There was a great variety of work assignment, such as repair of buildings and roads and the erection of garage and post exchange buildings. All occupational therapy was concerned with constructive activities that improved the installation. Group discussions and information and education activities were included in the program. Without too much difficulty a return-to-duty atmosphere was created. The results were soon evident in hospital statistics with a return-to-duty rate for nonpsychotic patients of over 50 per cent.

In March, 1943, plans were begun to have a separate and larger neurosis hospital. This was accomplished by the following November, and the 312th Station Hospital was made over into a neuropsychiatric unit. The plan of function that had been evolved at the 36th Station Hospital was adopted. After the initial work-up of each case, with a decision as to type of treatment, the patient spent between ten days and two weeks in the treatment section. Following this he was transferred to the training or rehabilitation wing, which was the needed step between hospital care and duty. At this hospital the return-to-duty rate averaged 80

per cent. It must be kept in mind that patients were received only after general hospitals had failed to return them to duty.

As a result of this experience and for various other reasons, it was decided that a similar neuropsychiatric unit should be formed to function on the Continent just in the rear of the Army. Accordingly, the 130th General Hospital, which arrived on August 1, 1944, was remade into a neuropsychiatric unit. As such it arrived in France on September 4, 1944, but because of loss of equipment was not able to start functioning until November 17. It was located at Ciney, Belgium. At first it was in a good position to receive all the neuropsychiatric patients coming out of the First and Ninth Armies, but because of an overflow of medical and surgical cases from the Liège area it did not begin to function as a neuropsychiatric unit until December 1. Then came the Battle of the Bulge, and by December 20 it was evident that this hospital would be in the center of the German drive. The commanding officer, Colonel Parsons, evacuated most of the patients and his staff, remaining behind with a few volunteers to care for nontransportable patients. Just before Christmas, the hospital was practically surrounded and the main road of escape was cut. German officers requested that adequate care be given wounded Germans, and this was done. Before the end of the year the German retreat had started, and by January 2, 1945, it was possible to bring back the staff and the hospital continued to function. At that time it was in front of the aid stations, but it soon became a field hospital, then a clearing station and later an evacuation hospital. During the latter part of January and during February it had to function as a regular station hospital. By the time its primary function as a neuropsychiatric unit was resumed the armies were beyond the Rhine and evacuation was being done almost entirely by air. This meant that all patients were flown beyond the area in which this hospital was located, the majority coming to Paris. During the periods that this hospital was able to function as a neuropsychiatric unit it was able to return 90 per cent of its patients to duty.

A similar unit, the 51st Station Hospital, came to the Continent from North Africa and served the Third and Seventh Armies. This hospital met the same fate that befell the 130th General Hospital. During the Battle of the Bulge it was necessary for it to do surgical work. Also, in the spring of 1944 patients were being flown from beyond the Rhine to the Paris area. This hospital when fully functioning as a neuropsychiatric unit also returned 90 per cent of its patients to duty. Before either of these hospitals could be moved forward, V-E Day came and the care of neuropsychiatric patients was centered in a general hospital in Paris.

Before leaving the subject of special neuropsychiatric units, mention should be made of the School of

Neuropsychiatry, which was really a part of the neuropsychiatric units. This was first opened in April, 1943, at the 36th Station Hospital under the direction of Lieutenant Colonel Jackson Thomas. At first neuropsychiatrists coming into the theater with general and station hospitals were given a one-month course. Along with this went courses for nurses and enlisted men working in neuropsychiatric sections of general and station hospitals. Also, during the summer of 1943, several courses, each lasting one week, were given for medical officers of ground force units. In September, 1943, Colonel Thomas was recalled to the Zone of the Interior, and it was not until late in the year that Major Howard Fabing arrived to take his place. The school was then moved to the 312th Station Hospital and practically all the instruction was given to front-line medical officers. Weekly classes were held for these men until the middle of July, 1944. As a part of the services to ground-force units it was necessary to train approximately 15 division psychiatrists. In addition to this, neuropsychiatrists, nurses and enlisted men from evacuation hospitals and other forward units were given definite courses of instruction. Approximately 700 medical officers who later worked in aid collecting or clearing stations were given the one-week course in what was called "first-aid psychiatry." The total number of persons attending this school was approximately 1200. A feature of the school was a weekly tent show in which conditions at the front were simulated and various syndromes of combat exhaustion were acted out and treated.

Before turning to the psychiatric services in the Army, mention should be made of the fact that there were psychiatric services in the two large reinforcement depots that handled patients going back to duty from hospitals. Also, the disciplinary training centers had psychiatric services. Mention should also be made of the Recovery Center, although there was no psychiatrist there. This was a training unit, with rather strict military discipline for the unwilling soldier. Trainees were carefully selected after thorough neuropsychiatric study, and it can be stated that this unit made good soldiers out of the majority of the trainees.

It has already been mentioned that the majority of medical officers who were dealing with casualties at the front had a course in first-aid psychiatry. This included prevention as well as early treatment. Also, line officers with combat units were instructed in various ways by Army and division psychiatrists. It can be stated that the division psychiatrist was the keystone of the psychiatric services in combat units. Every division had one. He functioned mainly at the level of the clearing station, where he had one or two tents separate from others for combat-exhaustion patients. An important part of his work was to see that the medical officers in front of him functioned efficiently. Quite early in

combat it was recognized that a division psychiatrist who was having a large percentage of men returned to duty from the clearing station was not doing a good job forward. Numerous examples could be given in which a division psychiatrist had a low rate of return to duty only because medical officers ahead of him sent him only the most difficult cases.

It was originally planned to have psychiatric services in evacuation hospitals, to carry on further study and treatment of patients whom the division psychiatrist had been unable to return to duty. This was the arrangement that existed in the North African theater until November, 1943. At that time the surgeon of the Fifth Army made the suggestion that the Army clearing station be used as a separate neuropsychiatric unit to relieve crowding in evacuation hospitals. The advantages of this arrangement were obvious, and this recommendation was brought back to the European theater of operations. Usually an evacuation hospital is looked on as being primarily a surgical hospital, and when it is crowded the transportable patients, especially the ambulatory ones are sent farther to the rear to make room for the seriously wounded.

Recognizing this possibility, the First Army some months before D Day organized an exhaustion center. This was a makeshift organization using a clearing company as the housekeeping unit, which was augmented by bringing in psychiatrists from evacuation hospitals on detached service. The plan of service and treatment was essentially the same as that described above for the larger neuropsychiatric hospitals in the communications zone. About two weeks after D Day, the exhaustion center of the First Army was functioning on the Continent. By the end of July, it was necessary to establish a second exhaustion center in the First Army, and early in August each of these exhaustion centers had approximately 1000 patients. It is obvious that the evacuation hospitals could not have handled this case load and that the majority of patients would have been evacuated to the hospitals in England.

The Ninth Army adopted this same plan, and the Seventh Army had been using such an arrangement before it came into France. The Third Army differed in that psychiatrists were kept in the evacuation hospitals, but these units were backed up by a special neuropsychiatric section in the convalescent hospital. For the Third Army with its particular type of combat, which was mostly rapid advance, this arrangement worked extremely well. In the end it was decided by most neuropsychiatrists who had had experience at the front that the exhaustion center should be established as an official part of the medical services of each army.

One could go into great detail in describing the various types of neuropsychiatric conditions seen under combat, but only a brief account can be given here. As is well known, the term "combat exhaus-

tion" was the only diagnostic label placed on the emergency medical tag of the neuropsychiatric patient at the front. This diagnosis was not changed unless he was evacuated. There is no doubt that in a few cases a more specific diagnosis could have been made right at first, but in the vast majority of cases this proved to be an excellent term. Naturally, the soldier read his diagnosis and the term "exhaustion" suggested to him a natural occurrence and speedy recovery. Treatment, too, was essentially that of overcoming an exhausted state and included sedation, food, sleep and reassurance. In the majority of conditions arising under combat conditions purely physical causative factors could not be separated from emotional and psychologic factors. The two were mutually contributory, one to the other. The vast majority of men coming back from combat with nervous symptoms were exhausted, and the majority of thoroughly exhausted men showed unsteadiness and even tremors, loss of efficiency, disturbed digestion and complaints of headache, bodily aching and loss of strength. These are the very symptoms seen in the more outspoken neuroses. In ordinary life, fatigue brings aching muscles, the tired business man is irritable, the exhausted child cannot fall asleep, strain often produces headache, and long hours of work lead to lowered efficiency. Usually the psychologic factors are more important, but there is such a thing as exhaustion of psychologic and emotional functions.

Any classification of type of cases is apt to be misleading because within a few hours or a day or two one type often changed into another, and still later and farther back one frequently saw a clinical picture that did not resemble the initial one.

By far the most frequent conditions found were the anxiety conditions. These can be divided into the highly acute and the subacute. In the highly acute conditions there was either panic or freezing. There is no need to describe these in detail, except to say they were extremely disconcerting to others. In the subacute conditions, rhythmic tremor was usually outstanding and a startle reaction was prominent. These soldiers looked exhausted and gave a history of having had little sleep and a loss of appetite. For many of them, battle dreams were quite disturbing.

At the front, clear-cut hysterical conditions were not so frequent as might have been expected, judging from the history from the last war. The obvious hysterical paralyses were in the minority, and the most frequent hysterical symptom was amnesia. After this came loss of voice or stuttering, and there were occasional patients with hysterical blindness or deafness. Not infrequently a patient who had first appeared with an anxiety condition later showed some hysterical symptoms as his outspoken anxiety symptoms diminished.

After a unit had been in combat for a long time, the proportion of patients with what was called "re-

active depression" increased. These syndromes came mostly in conscientious noncommissioned officers who had been at the front for a long time. They appeared definitely exhausted and depressed, with self-accusatory trends. Mention should also be made of the pseudopsychotic cases. These patients seemed hallucinated and disoriented and sometimes presented a typical catatonic picture. The psychotic symptoms rapidly subsided but often left anxiety or hysterical syndromes.

In discussing the topic of treatment it is appropriate to consider prevention because there is no distinct dividing line between prevention and treatment. As stated above, line officers as well as all division medical officers had some indoctrination in prevention and early recognition of combat exhaustion, but perhaps not enough. In this training, emphasis was placed on the quality of leadership as a primary factor in prevention. It was considered important that soldiers be fitted into their proper assignment so the job was neither too big nor too little for their abilities and training. Selection, classification and assignment was considered a continuing process in all units. Adequate training, indoctrination and discipline were important because they added to the soldier's confidence in taking care of himself. Another item in prevention was the way in which reinforcement troops were introduced into the unit during fighting. The problem of providing adequate rest periods for smaller or larger units was a topic of constant discussion. Rest periods were instituted wherever the tactical situation allowed. It was considered better to do this than to wait for the soldier to become a medical casualty. Such rest periods gave him something better to look forward to than death, maiming or a psychiatric breakdown. The medical officer with combat troops was schooled to be on the lookout for the man who was getting jumpy, going off by himself, becoming sleepless, losing his appetite or showing other symptoms of undue strain. He was urged to see that his men were as comfortable, well fed and clean and dry as possible under any given set of circumstances. He was also told that a good medical officer had an interest in the soldiers' everyday life, in their sports and in their equipment and that he had to share their dangers and hardships.

Concerning treatment more specifically, the front-line medical officers did recognize early symptoms, and the usual procedure was to send the soldier back to the kitchen area or some similar place where he could have a good sleep, perhaps with a little sedation, one or two hot meals and a chance to wash, shave and dry his clothing. Of course the personal contact, the explanation and reassurance given and the temporary relief from constant vigilance were important factors in this first-aid work. Just how many men were so treated and returned to duty the following day is not known because no records could be kept, but there were cer-

tainly many of them. Several division surgeons told me that at least 50 per cent of the combat-exhaustion patients were returned to duty in this way.

If the symptoms were too pronounced for this simple treatment, the soldier was evacuated, under sedation, to the clearing station. Sedation during this process seemed to render the job easier and made the patient more comfortable. Certainly patients arriving at the clearing station under sedation were in much better condition than those sent back without it. Also, it appeared that fixation of symptoms was in some measure prevented.

At the clearing station the patient was kept under the care of the division psychiatrist for two to four days. For the majority of patients so held, sleep during the first twenty-four to thirty-six hours was assured, with due attention to nutrition. Sodium amytal was used, so that the patients slept through the night and had a nap in the forenoon and afternoon. At least another day was given to occupation, recreation and group or individual talks. In some divisions more extensive rehabilitation programs were tried. At this level, hysterical symptoms usually responded readily to suggestive therapy, with or without the aid of drugs.

At the exhaustion center the patients could be held longer—for seven to ten days—and the treatment, especially the rehabilitation program, could be carried out much more thoroughly. Moderate sedation was used for the first few days, and occasionally modified insulin therapy was employed. Group psychotherapy and individual psychotherapy where indicated were considered of the greatest importance.

Reference to treatment in the neuropsychiatric units in the Zone of Communications has already been made. Moderate sedation therapy was extensively employed, but this was frequently com-

bined with modified insulin therapy. Group and individual psychotherapy often started with the above treatment and was always carried on so far as necessary or so far as time permitted. In individual psychotherapy, Sodium Pentothal abreaction was used more frequently than was hypnosis. Some neuropsychiatrists thought that group psychotherapy was the most valuable of all forms of treatment. Others thought that in the majority of cases the individual working out of problems, with or without drugs or hypnosis, was necessary. The modified insulin therapy, which was undoubtedly instrumental in the gain in weight and physical well-being, could not have been left out in the majority of cases. It can be added that without the rehabilitation program the return-to-duty rate would not have been nearly so high.

Regardless of what type of treatment was the most efficacious, it is known that within Army psychiatric services, 60 per cent of the patients were returned to active duty, and that the majority of them resumed combat duty. This does not count the patients who were returned to duty up forward at the aid stations. At this rate, 40 of every 100 patients came back to the Zone of Communications. There the neuropsychiatric hospitals were able to return approximately 80 per cent to duty, but mostly noncombat duty. This leaves only 8 or 10 of the original 100 patients for evacuation to the Zone of the Interior. Among these were a few psychotic and epileptic patients and others who could not possibly be reclaimed for service.

There are many more interesting topics that might be discussed, such as morale, individual case studies, motivation of the soldier, selection and placement and personality factors in those suffering breakdowns. All these topics deserve separate papers. It is hoped that the above description has given some idea of the over-all developments in neuropsychiatry in the European Theater of Operations.

INFECTIOUS DIABETIC GANGRENE OF THE SKIN OF THE NECK

Report of a Case

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WHEN diabetes mellitus and gangrene are associated, one usually thinks of this combination in relation to the extremities, along with arteriosclerotic peripheral vascular disease. Gangrene of other parts of the body is considered to be a rare complication of diabetes mellitus. Nevertheless a growing, if scattered, literature on this complication is accumulating. There has been reported diabetic gangrene of the nasal septum and turbinates,¹⁻⁵ the orbit and nares,^{5, 6} the nares alone,^{7, 8} the right half of the tongue,⁶ the lip,⁹ the skin of the entire body,¹⁰ the face,^{5, 6, 11-13} the lung,¹⁴ the vulva¹⁵ and the glans penis and urethra.¹⁶

It is our purpose to report a case of diabetic staphylococcal gangrene of the skin of the entire neck. This complication of diabetes mellitus presented some interesting features regarding the differential diagnosis, the prognosis and, in particular, the treatment.

CASE REPORT

J H, a 51-year-old salesman, was admitted to the South Nassau Communities Hospital in Rockville Centre, New York, on May 5, 1944. His illness began 10 days before admission, when he noted some pain in the back of the neck, which progressed to redness and swelling. The pain and swelling, which had begun at the nape of the neck, spread over the entire neck, and the patient began to run a fever. He treated himself with hot compresses, and 2 days before admission consulted one of us (R T D), who suspected a beginning carbuncular lesion secondary to diabetes mellitus and advised hospitalization. No history of trauma could be obtained.

The past history revealed diabetes of many years' standing. Twelve years previously the patient had an abscess on his forehead, which was extremely painful and slow to heal. The family history was noncontributory.

Physical examination revealed an obese, stocky man. It was essentially negative except for the obesity, a heart that was enlarged to the left, a blood pressure of 180/94 and the neck lesion. The patient appeared acutely ill.

The lesion on the neck extended from slightly above the hair line to the shoulders and laterally around to the line of the ear lobes on both sides. It was raised but flat and was red and brawny in appearance. There was no sharp line of demarcation. There was no evidence of the typical multiple-headed boil characteristic of carbuncle. The red-cell count was 4,500,000, and the hemoglobin 12.6 gm. The white-cell count was 25,000, with 80 per cent neutrophils, 13 per cent small lymphocytes, 5 per cent monocytes, 1 per cent basophils and 1 per cent eosinophils. The urine contained 10 per cent sugar and gave a +++ test for acetone, the test for diacetic acid was negative. The blood-sugar level was 200 mg per 100 cc.

The patient was treated vigorously for diabetic acidosis with insulin and intravenous fluids. Seven days after admission the urine was clear of sugar and acetone. The patient ran a septic temperature ranging from 99 to 104°F.

Shortly after admission the red, brawny area suddenly became cyanotic and in 24 hours it became gangrenous. The gangrene was sharply demarcated. Small, scattered crops of blebs filled with fluid appeared, these soon broke and began to discharge pus. A culture of this material revealed *Staphylococcus albus* and *Staph aureus*. The patient was seen by one of us (J M), at which time a diagnosis of diabetic staphylococcal gangrene of the skin was made. Conservative treatment was advised, inasmuch as the diagnosis of carbuncle of the neck had been entertained and surgical treatment was anticipated. The lesion did not present any of the characteristics of the multiple-headed boil discharging pus from many openings that is usually associated with carbuncle.

Further laboratory studies of the blood and urine are shown in Table 1.

At first, borie acid wet dressings were applied locally to the gangrenous areas with the intention of localizing the infection, without effect. For a while there was mild drainage from the blebs.

On the 5th day after admission, treatment with penicillin was begun. A dose of 1,300,000 units was given intramuscularly in the buttock and locally around the lesion dur-

TABLE 1 Laboratory Data

	URINE			BLOOD SUGAR
	SUGAR	ACETONE	DIABETIC ACID	
5-8-44	4%	++++	++	mg /100 cc
5-11	2%	++	0	
5-12	Trace	0	0	
5-13	0	0	0	
5-15	0	0	0	220
5-18	0	0	0	
5-22	0	0	0	190
5-26	0	0	0	102

ing a period of 3 days. In the last few days of hospitalization only dry dressings were used. The temperature, which had been ranging up to 104°F, dropped to 101.2° for 2 days and after the 7th day averaged 100.4° for 3 days and 100° for 10 days. It was normal on the day of discharge, March 25. The patient left the hospital with the entire back of the neck covered with a typical dry, purple gangrene (Fig 1), which was as extensive as the day the neck became gangrenous.

The patient was last seen on July 11, 1944, at which time the faintest blush could be seen where the former area of gangrene had been (Fig 2). There were a few scattered punctate areas, where former blebs were still in the process of granulation. Aside from this the skin appeared normal. The diabetes was under control, and the patient was quite well.

DISCUSSION

The clinical diagnosis of diabetic staphylococcal gangrene of the skin offers little difficulty once the gangrene appears. In the early stages of the infection it may be mistaken for erysipelas. This diagnosis has been made on several occasions.^{6-8, 11} Another lesion that resembles erysipelas in its early stages and later becomes gangrenous is hemolytic streptococcus gangrene of the skin, described by Meleney.¹⁷ The differentiation is established by bacteriologic examination.

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The mechanism producing this type of gangrene is distinct. Buerger,¹⁸ in describing the diagnosis and pathologic process of the so-called "diabetic gangrenes," draws attention to four distinct varieties of the disease—the arteriosclerotic, the thrombotic, the embolic and the thromboangitis obliterans form. The essential features of these types may be described briefly as follows. The arteriosclerotic

thrombus formation. This type likewise is most frequent in the peripheral vessels. Embolic gangrene is a sequel to the lodging of an embolic mass, which is frequently carried from some distant focus and when infected leads to suppuration, abscess formation and gangrene. This type of gangrene may occur in vessels that are otherwise normal. Thromboangitis obliterans is characterized by in-



FIGURE 1 Photograph Taken Several Days before Discharge from the Hospital

type occurs in persons of advanced years and involves the larger arteries, especially those of the periphery, in vessels that are the site of advanced arteriosclerosis. It is characterized by proliferation of the endothelial lining, with an increase of the subendothelial connective tissues, as well as by fatty degeneration, with the deposition of fat, lipoids and cholesterol. The necrosis is associated with atrophy and calcification of the tunica muscularis and the tunica adventitia, leading to occlusion.

Thrombotic gangrene occurs in vessels that are the site of arteriosclerosis of a mild degree and is characterized by sudden occlusion as a result of

involvement of the superficial veins and arteries by an acute inflammatory process, resulting in thrombus formation and subsequent occlusion.

There are several predisposing factors to be considered in the production of diabetic gangrene of the skin. First of all, there is the diabetic patient, who is always susceptible to infection. Trauma to the skin, however slight, may be a precipitating factor. The ever-present staphylococcus needs little more encouragement for invasion under such circumstances. The resulting brawny inflammation and edema may produce an arteritis of the terminal ves-

sels in the skin, with thrombosis and subsequent gangrene of the parts supplied.

The edema beneath the surface of the lesion may lend a misleading appearance regarding the depth of the gangrene. The gangrene in the present case must have been superficial indeed to have cleared

a large crater with undermined edges. Occasionally in this type of lesion one sees small areas of gangrene of the skin about the edge of the crater.

Unlike diabetic gangrene of the extremities, age apparently plays no role in this type of gangrene. The youngest patient on record was four years of

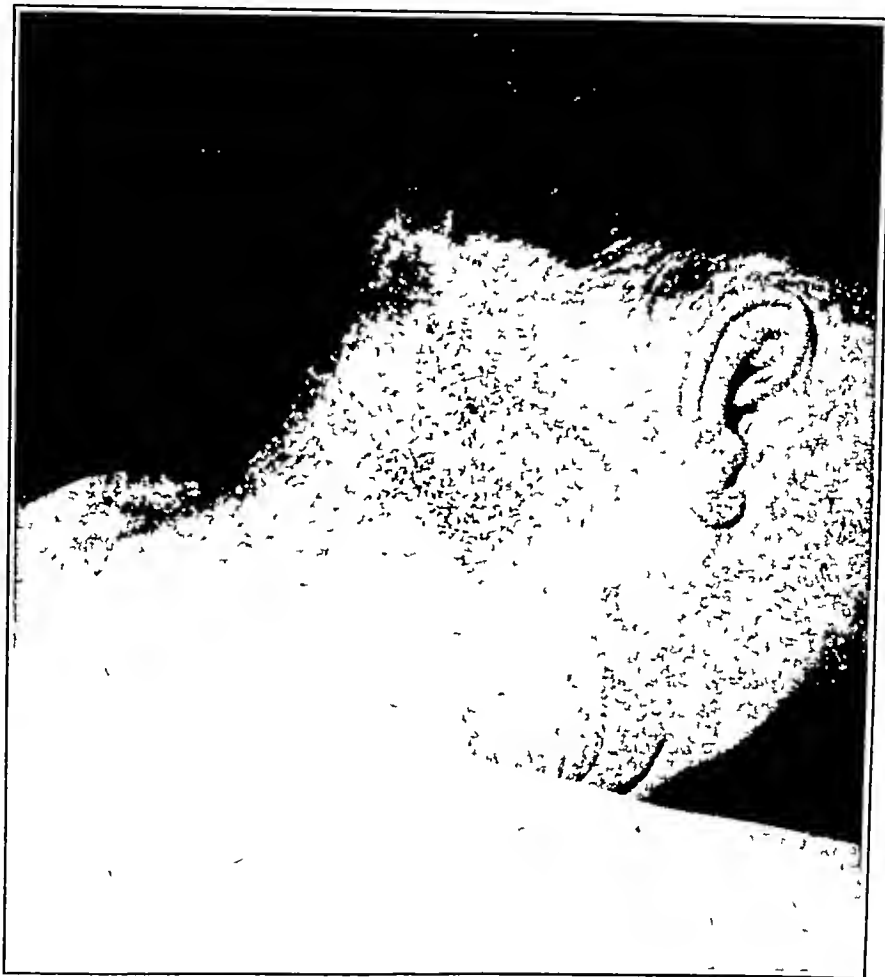


FIGURE 2 Photograph Taken a Month and a Half after Discharge from the Hospital

up without the skin's sloughing out *en masse*, as might have been expected from its appearance. It was only in the scattered areas where the blebs containing clear fluid appeared, later to discharge pus, that the gangrene was deep enough to produce actual necrosis of the entire depth of the skin, with subsequent replacement by scar tissue. These areas were small as compared to the actual amount of skin surface involved. From a pathological and clinical point of view, this tends further to distinguish this lesion from carbuncle, in which there is usually a large central necrotic area discharging pus from many small openings in the skin. This deep necrotic lesion if left alone eventually sloughs out and leaves

age, followed by 1 eight years and 2 ten years of age. The oldest patient was sixty-five years of age.

The prognosis of diabetic gangrene of the skin is uniformly favorable. The only exceptions are the lesions that involve the cheek over the malar areas. The lesion in this location easily spreads into the blood vessels leading inside the skull, resulting in cavernous-sinus thrombosis, brain abscess and meningitis or drainage into the general circulation with bacteremia and metastatic abscesses. All these patients have died.^{5, 6, 11, 12} All patients with lesions involving other areas about the head, the nasal septum and turbinates, the hard palate, the eyelids, the skin of the nose and ears, the lip and

the tongue have recovered, with one exception (Bowers's⁵ Case 1), and this death occurred in the pre-insulin era

The complications following diabetic gangrene of the body surfaces depend on the extension of the lesion to adjacent structures. Thus, in Morris's¹ case, involvement of the turbinates and septum was complicated by involvement of the adjacent sinus and the third, fourth and ophthalmic branch of the fifth and sixth nerves. In Briers's case, involvement of the skin of the ear and the area anterior to it was complicated by involvement of the fifth and seventh nerves. In Ardeshir's⁸ case, gangrene of the skin of the nose was accompanied by destruction of the underlying cartilage of the nasal alae, whereas Wood's⁷ case resulted in spontaneous amputation of the entire nose and the loss of the nasal septum and the nasal processes of the superior maxilla and nasal bones. Goldberg's³ case of gangrene of the nasal cartilage and right middle and inferior turbinates resulted in osteomyelitis of the right orbit, and Speidel's⁴ case of gangrene of the nasal septum ended with atrophy of the right optic nerve. Millett¹¹ has shown in his 2 cases of gangrene of the cheek that where the extension of the infection had involved the general circulation, positive blood cultures for staphylococci were obtained, and that in the case that came to autopsy metastatic abscesses were found in the lungs. The organisms cultured from the cheek lesion and from the blood stream were identical.

The proper treatment of diabetic gangrene of the skin is both general and local. The diabetes and any acidosis present must be controlled by insulin, fluids and dextrose. Local treatment should in the main be conservative. Watchful waiting is probably the procedure of choice. Wet dressings and careful removal of slough as it occurs can be done as needed. Penicillin may well prove to be a life-saving procedure when septicemia is present. It should be used at all times in these cases, since it

may well prevent such a complication. Drastic surgery should not be done, since it may open up new channels for systemic invasion by organisms.

SUMMARY

A case of extensive infectious diabetic gangrene of the skin involving the entire neck is reported. The patient recovered.

Infectious diabetic gangrene of the skin may be considered as a separate clinical entity having a distinct clinical course and a definite pathology.

In differential diagnosis it must be considered with erysipelas in its early stages and carbuncle in its later stages.

Conservative treatment should be given. Penicillin may be life-saving in preventing septicemia or in overcoming it when it occurs.

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MEDICAL PROGRESS

ENDOSCOPY*

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ALTHOUGH endoscopy may seem to be a narrow specialty, many of the most interesting diagnostic problems in the hospital eventually come to some form of endoscopic examination. As will be seen in the following review, these include many pulmonary problems that may need bronchoscopic study, gastrointestinal problems, which often require a direct inspection by esophagoscopy or gastroscopy, and various abdominal conditions, such as hepatomegaly, unexplained ascites and abdominal or pelvic masses, which may be satisfactorily studied by peritoneoscopy.

BRONCHOSCOPY

Congenital Anomalies

Ferguson and Neuhauser¹ report 5 cases of agenesis of the lung diagnosed during life by bronchoscopy, followed by iodized oil roentgenograms of the tracheobronchial tree. These cases illustrate the fact that this deformity is not incompatible with a normal existence, since 4 of the patients are living normal lives and are not handicapped by their defect.

Gross and Lewis² report the case of a four-year-old child who had a large opening in the anterior mediastinum, a free interpleural communication and an anomaly of the right upper-lobe bronchus. The bronchus was not more than 4 or 5 mm in diameter. When freed adequately from overlying tissue so that it could be palpated, it was found to be soft and apparently devoid of cartilage in the exposed section. This deficiency allowed the airway to collapse in such a manner that air entered the upper lobe and became entrapped therein. Marked emphysema of the right upper lobe allowed it to protrude through the mediastinal opening and invade the left pleural cavity. The patient had intermittent attacks of severe respiratory distress, dyspnea and cyanosis, which were completely relieved by simultaneous closure of the anterior mediastinal defect and removal of the anomalous right upper lobe. This is apparently the first recorded case of surgical repair of an anterior mediastinal defect. In retrospect, one wonders whether this patient might not have been cured by right upper lobectomy alone. Although this possibility is freely admitted, it seemed to the authors at the time of

operation that limitation of the surgical correction to lobectomy might be followed by subsequent distention of the left lung so that it would project through the free space in front of the heart. In order to prevent any such shift, it was believed that obliteration of the anterior mediastinal space was necessary to ensure against any recurrence of respiratory difficulties.

Gross³ has reported a case of tracheal obstruction from a vascular ring relieved surgically. The case was that of an infant who was proved to have tracheal compression from a vascular ring within the mediastinum. The obstruction was particularly troublesome because of repeated attacks of superimposed tracheitis, for which the patient was hospitalized on four different occasions. Roentgenologic studies showed evidence of a vascular ring, and at operation the vessels were suitably divided to allow sufficient room for the trachea. The patient tolerated this surgical procedure extremely well and had marked alleviation of symptoms. The detection of a vascular ring is apparently not difficult. Since in the vast majority of these patients some portion of the ring passes behind the esophagus, fluoroscopic observation after a swallow of barium should show indentation of the posterior wall of the esophagus. If such esophageal deformity is found, the trachea can be studied by the introduction of lipiodol and by appropriate film studies in the anteroposterior and lateral views to detect any constriction of the trachea that may exist. Vascular rings do not always give rise to important clinical symptoms, but when the compression of the trachea is great enough to give rise to respiratory distress, surgical division of some portion of the ring should offer an excellent chance for relief of symptoms.

Bronchiectasis

Stookey, Lockwood, Mantz and Buckingham⁴ studied penicillin therapy in bronchiectasis. The bacteriologic findings demonstrated that little aid resulted from the use of sulfonamide drugs. Staphylococci were the most consistent and persistent of the pathogens. The most frequent combination was one form of the staphylococcus with *Streptococcus viridans*. Twenty-one patients received an average of 1,000,000 units of penicillin by intramuscular and intravenous injection in eight to ten days. The volume of sputum was not influenced,

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but from a clinical standpoint cases showed evidence of improvement. Chronic bronchitis associated with periods of activity and remission gave the best hope of therapeutic response. The true bronchiectatic patient showed little or no response to penicillin. I believe, however, that in inoperable cases of bronchiectasis, penicillin inhalations combined with postural drainage and bronchoscopic aspiration offer the best hope of palliative relief.

Thomas, Van Ordstrand and Tomlinson⁵ studied 75 cases of bronchiectasis treated by sulfonamides or allergic management or both. In 57 cases, lipiodol bronchography and bronchoscopy established the diagnosis. Twenty-three of these patients showed definite improvement, with a reduction of cough and expectoration while under treatment. In 31 cases, combined allergy and sulfonamide therapy was used. Twenty-six patients showed 25 to 100 per cent improvement in cough and expectoration.

In a symposium on bronchiectasis by members of the Mayo Clinic, Hinshaw⁶ calls attention to the fact that bronchiectasis should not be discussed without mention of the many pitfalls in diagnosis. Obstructive lesions, such as bronchiogenic carcinoma, bronchial adenoma, foreign bodies and inflammatory stricture of a bronchus, should also be emphasized. Furthermore, tuberculosis may occur in any portion of the lung, and when it is present in a lower lobe it may resemble bronchiectasis.

Olsen⁷ believes that foreign bodies, bronchial tumors, broncholiths, bronchial strictures and bronchial compression must be ruled out by bronchoscopic examination. It is his opinion that bronchoscopy should be performed in the majority of cases of suspected bronchiectasis. Furthermore, the bronchoscopist can frequently play an important part in the prevention of bronchiectasis. The timely removal of an aspirated foreign body almost invariably prevents the development of pulmonary suppuration. Bronchial obstruction due to neoplasms or broncholiths may be relieved by bronchoscopic means, and in many cases permanent damage to the bronchi may be avoided. Pulmonary atelectasis not infrequently occurs after surgical procedures when thick, tenacious secretions become impacted in the bronchi. Bronchoscopic aspiration of these secretions should be carried out early if bronchial disease and pulmonary complications are to be prevented. When a pneumonic process fails to resolve, bronchial complications should be suspected.

Clerf⁸ thinks that bronchoscopy is of value in bronchiectasis only as a diagnostic aid and as a palliative measure preparatory to carrying out surgical treatment. In cases of obstructive bronchiectasis a diagnostic bronchoscopy is absolutely indicated before surgical intervention, since there may be present a foreign body, stricture of the bronchus or benign neoplasm, any of which may seriously complicate the surgical result. All cases of unilateral bronchiectasis should be considered as

surgical problems, since no cure can be obtained by bronchoscopy alone. Its use would, therefore, deprive of a cure a patient suitable for surgical treatment.

Foreign Bodies

Hammond⁹ reports an emergency cervical mediastinotomy in a case of massive mediastinal and subcutaneous emphysema secondary to removal of a foreign body from the bronchus. The foreign body was a piece of apple, found in the orifice of the left main bronchus. A piece of it was removed with forceps, following which the remaining portion was suddenly and forcibly expelled through the bronchoscope. Twenty minutes later the author was urgently called to the pediatric floor to see the patient. Swelling of the tissues of the neck and the upper chest was noted, following which respirations became labored and the abdomen began to swell. The picture was extraordinary. The whole body was emphysematous, particularly the abdomen, which had the appearance of a balloon that was rapidly becoming overinflated with each respiration. The eyelids were bulging, and the scrotum was as large as two adult fists. Creptitation was noted over the entire body, extending to the fingers and toes. Immediate cervical mediastinotomy was decided upon. A midline incision was made from the thyroid notch to the sternum. There was a sudden gush of air from the subcutaneous tissues. Abdominal tension was relieved by multiple needle punctures under the skin. Within a few minutes, respirations appeared normal, and the wound was lightly packed with vaseline iodoform gauze and the patient returned to bed. Hammond concludes as follows:

A check-valve obstruction of the bronchus by a vegetal foreign body is reported in a child. The increased pulmonary pressure secondary to a foreign body in the bronchus was aggravated by the straining during bronchoscopy. A rupture of the alveoli followed, with the escape of air along the blood vessels to the mediastinum, following which there was generalized extension of air over the whole body by way of the blood vessel sheaths. The rapid and continuous passage of air into the body tissues led to marked ballooning and extreme cyanosis. Fatal termination was prevented by an emergency cervical mediastinotomy.

Adenoma

Clerf⁸ calls attention to the fact that in the earlier cases of adenoma it was not known that many of these tumors presented an extrabronchial as well as an endobronchial portion. Bronchoscopic methods of therapy were therefore instituted, and remarkably good results were secured in a number of cases. If one can determine by bronchoscopy and tomographic studies that the tumor is endobronchial, it may be successfully treated by diathermy. If there is an extrabronchial portion, however, surgical extirpation will ultimately become necessary. Clerf has found it necessary to have a number of his earlier cases submit to surgical treatment. Although there are observers who believe that this is

a malignant tumor, few cases of implants either in the lung or in other tissues have been recorded

Jackson, Konzelmann and Norris¹⁰ have studied the clinical features of 20 cases of so-called "adenoma of the bronchus." They believe that infiltration of the bronchial wall is possible, but that it is sufficiently infrequent and limited when it does occur so that endobronchial removal is justified when it can be done, it being admitted that complete removal by this means is often not possible and that obviously incompletely removed tumors will recur. That these tumors may undergo malignant change must be admitted. The experience of the Jackson Clinic indicates that malignant change is infrequent. These authors do not believe that adenomas have any inherent tendency to metastasize or become malignant in any other way. None of their patients have shown such a course, although a number have been under observation for ten years or longer. The possibility of extrabronchial growth of adenomas, producing a so-called "collar-button" lesion with the larger part outside the bronchus, is recognized but is thought by many to have been overemphasized. Bronchoscopic treatment by forceps removal, electrocoagulation and aspiration is indicated as the first step in all cases, it is curative in some and palliative in others. In cases in which there is atelectasis or bronchiectasis, a preoperative course of bronchoscopic treatment is indicated, even if lung resection has been definitely decided on or is to be considered at a later date. Lobectomy or pneumonectomy is indicated when bronchoscopic cure of the bronchial lesion seems impossible, or when prolonged bronchial obstruction has resulted in serious permanent damage to the distal portion of the lung.

Graham and Womack¹¹ have also discussed so-called "bronchial adenoma," stating that the chief clinical problem that these tumors present concerns the question of whether they are to be regarded as either actually or potentially invasive in nature or should be considered purely benign in type. It is difficult to understand how there could be any controversy on the point at this time. If one accepts as criteria of malignancy invasion of adjacent tissues, involvement of regional lymph nodes and metastasis to distant organs, then in the light of a considerable amount of published experience one cannot deny that there have been authentic cases in which these tumors have become malignant, for many cases have been recorded in which these three criteria mentioned have been present. In view of the well established malignant potentialities of bronchial adenoma, the principles of treatment become clear. It seems to Graham and Womack that radical surgical removal is the procedure of choice. Because of the frequency with which one finds a large portion of the tumor outside the bronchus, it appears that only rarely can it be completely removed through the bronchoscope. In many cases

such an attempt is particularly hazardous because of the danger of perforation of the bronchus. If the tumor is not completely removed, there will always be the danger of a later invasion by the part left behind, as in the case cited by Burrell¹² and that of Graham and Womack. An additional objection to the local removal of the tumor is the uncertainty in many cases of whether it is actually malignant at the time of operation, and if so, the extent of its spread. The piece of tissue that has been removed by bronchoscopy for biopsy may not show clear evidence of malignancy, even when the tumor has already invaded neighboring tissues or regional lymph nodes. Still another reason why bronchoscopic removal is likely to be unsatisfactory is that there is often an associated bronchiectasis, supposedly due to the bronchial obstruction produced by the tumor. Undoubtedly lobectomy sometimes proves to be an adequate operation, but it is Graham and Womack's opinion that often it is not adequate because of the location of the tumor. They therefore prefer the operation of total pneumonectomy for these cases. The removal of possibly involved regional lymph nodes can be much more satisfactorily accomplished in this way. In good-risk patients there is scarcely if any greater danger from the operation of total pneumonectomy than from lobectomy. In conclusion, these authors are in disagreement with Jackson,¹⁰ believing that the frequent inability to determine from a biopsy specimen whether the tumor has already become malignant makes an attempt at local removal through the bronchoscope both unwise and dangerous. They claim that total pneumonectomy is the procedure of choice.

In a discussion of the above paper, Alexander states that he and Dr. Haight and their pathologist, Dr. Carl Weller, all agree that so-called "adenoma" is a Grade 1 carcinoma.¹³ They believe that the risks of hemorrhage, of recurrence and particularly of transition to a more active type of malignancy than Grade 1 carcinoma, or from the fetal stage to a true carcinoma stage, together with the great ultimate risk to life of suppuration of the lung and pleura, far outweigh the risks of expertly performed lobectomy or pneumonectomy.

In reply to Alexander's remarks, Jackson¹³ stated that in his cases he had not had any cases of "frightful" hemorrhage from an adenoma. He believes that the way to minimize the risk from hemorrhage is not to try to do too much at one time. Biopsy is enough for the first time, then electrocoagulation, subsequently alternating forceps removal with electrocoagulation at appropriate intervals, removing the obstructive lesion in a series of bronchoscopies rather than trying to effect a cure in one treatment.

Holinger¹³ states that in his experience the question of hemorrhage is one that influences the choice of therapy. If a tumor has a tendency to bleed profusely when efforts are made bronchoscopically to

free the affected bronchus, bronchoscopic removal is discontinued and surgical resection is advised. He believes that cases with a marked tendency toward bleeding are definitely not bronchoscopic problems.

In a continuation of this discussion, Graham¹³ states that bronchial adenomas are potentially malignant. In his clinic he knows of more than 10 cases in which there have been regional or distant metastases from tumors that began as adenomas with a long history.

Tyson and Milliken¹⁴ think that recently there has been a swing toward the viewpoint that adenoma is usually benign but may become malignant. Because of irreparable lung damage beyond the tumor and the possibility of extrabronchial extension of the tumor, they concluded that in the case reported a pneumonectomy was necessary. Examination of the surgical specimen showed that the adenoma had protruded through the posterior surface of the bronchus in a collar-button manner, the extrinsic portion being about a fourth as large as the portion within the lumen. The middle and lower lobes were completely obstructed and their bronchi were filled with mucopurulent material. The patient's only symptom four years after the operation is some shortness of breath and wheezing if she walks rapidly up a steep hill. She is able to carry on her housework and her duties as a telephone operator without respiratory embarrassment.

Chamberlain and Gordon¹⁵ also favor pulmonary resection for bronchial adenoma. Although these tumors were first treated by endobronchial removal, these authors believe that pulmonary resection is preferable for the following reasons. It offers a definitive cure, the hazards associated with the damaged lung distal to the tumor are avoided, and some of these tumors are potentially malignant and occasionally metastasize. Endobronchial removal is indicated in four groups of cases — those that are not reasonable surgical risks, those that involve the trachea, those with abscess distal to the tumor, which are best prepared for subsequent resection through improvement in the bronchial drainage, and the rare cases in which the tumor is entirely within the bronchus, easily accessible and attached by a long, slender pedicle. These authors report 10 cases all having the same fundamental features characteristic of bronchial adenoma, the extrabronchial portion in each case being larger than the endobronchial element. Pulmonary resection completely removes the tumor and the irreparably damaged lung distal to the obstruction. At operation mediastinal nodes should also be removed, since they are occasionally involved. Endobronchial therapy, although favorably reported on, lacks the advantage mentioned and has some disadvantages. It requires repeated manipulations, since local recurrences are frequent, and the risk of severe hemorrhage is always a consideration. Cicatrization may

occur following repeated bronchoscopic treatments, with or without the use of radon. Such scarring and stenosis interfere with the cleansing mechanism of the bronchus — ciliary action and bronchial peristalsis — and predispose to pulmonary suppuration. The principal therapeutic objective is maintaining a patent airway if cicatricial stenosis is substituted for an obstructing tumor. Even in the absence of scarring and local recurrence stenosis may occur.

Clerf and Bucher¹⁶ have noted in cases treated by bronchoscopy that after years of freedom from symptoms and no recurrence of the growth endobronchially, there is progressive narrowing of the bronchial lumen by either an intramural or an extrabronchial growth. It is of interest that the cause of death in these cases is usually due to pleural and pulmonary suppuration, secondary to the bronchial obstruction, and occasionally to hemoptyses following bronchoscopic manipulation, yet there is no record of a death due to metastases.

Harrill¹⁷ reports a case of adenoma of the trachea, the most prominent clinical feature of which was tracheal obstruction. Adenoma arising from the upper part of the trachea is rare. A tracheotomy was done, and the mass was later removed by forceps through a tracheoscope.

Cylindroma

McDonald, Moersch and Tinney¹⁸ have reported 6 cases of cylindromas of the bronchus. Histologically, cylindroma presents a different appearance from that of adenoma of the bronchus and appears to be more allied to mixed tumors. The clinical course is remarkably similar to that of adenoma. The bronchoscopic appearance of the tumor is also similar to that of adenoma. Bronchiectasis and lung abscess are frequent sequelae to the long-standing obstruction produced by the tumor.

Carcinoma

Overholt and Wilson¹⁹ have recently discussed silent and masquerading intrathoracic lesions. They believe that the figures regarding the bronchoscopic diagnosis of bronchiogenic carcinoma are misleading. They state that the medical literature abounds with statistics indicating that 70 to 75 per cent of all bronchiogenic carcinomas originate in the major bronchi and are thus visible through the bronchoscope and accessible for biopsy. They believe that these figures are false when applied to early carcinoma of the bronchus. If bronchoscopy is performed early, it is negative in 40 per cent of the cases because the site of origin is beyond bronchoscopic view. Bronchoscopy is, therefore, an unreliable guide when the results are negative, since it does not in any way exclude the presence of the tumor immediately beyond the vision of the bronchoscopist. They believe that in the diagnosis of early cancer bronchoscopy is about 50 per cent inefficient, furthermore, a negative bronchogram in no way

a malignant tumor, few cases of implants either in the lung or in other tissues have been recorded.

Jackson, Kosselmann and Nemis¹¹ have studied the clinical features of 55 cases of so-called "adenoma of the bronchus." They believe that infiltration of the bronchial wall is possible but that it is sufficiently infrequent and limited when it does occur so that endobronchial removal is justified when it can be done, it being admitted that complete removal by this means is often not possible and that obviously incompletely removed tumors will recur. That these tumors may undergo malignant change must be admitted. The experience of the Jackson Clinic indicates that malignant change is infrequent. These authors do not believe that adenomas have any inherent tendency to metastasize or become malignant in any other way. None of their patients have shown such a course, although a number have been under observation for ten years or longer. The possibility of endobronchial growth of adenomas, producing a so-called "collar-bronchus" lesion with the larger part outside the bronchus, is recognized but is thought by many to have been overemphasized. Bronchoscopic treatment by forceps removal, electrocoagulation and aspiration is indicated as the first step in all cases; it is curative in some and palliative in others. In cases in which there is atelectasis or bronchiectasis, a preoperative course of bronchoscopic treatment is indicated, even if lung resection has been definitely decided on or is to be considered at a later date. Lobectomy or pneumonectomy is indicated when bronchoscopic cure of the bronchial lesion seems impossible or when prolonged bronchial obstruction has resulted in serious permanent damage to the distal portion of the lung.

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In a discussion of the above paper, Alexander states that he and Dr. Haight and their pathologist, Dr. Carl Walker, all agree that so-called "adenoma" is a Grade I carcinoma.¹⁴ They believe that the risks of hemorrhage, of recurrence and possibility of transition to a more active type of malignancy than Grade I carcinoma, or from the final stage to a more carcinoma stage, together with the great ultimate risk to life of suppuration of the lung and pleura, far outweigh the risks of expertly performed lobectomy or pneumonectomy.

In reply to Alexander's remarks, Jackson¹⁵ stated that in his cases he had not had any cases of "highly fatal" hemorrhage from an adenoma. He believes that the way to minimize the risk from hemorrhage is not to try to do too much at one time. Biopsy is enough for the first time, then electrocoagulation, subsequently electrosecting forceps removal with electrocoagulation at appropriate intervals, removing the obstructive lesion in a series of bronchoscopic rather than trying to effect a cure in one treatment.

Hilfinger¹⁶ states that in his experience the question of hemorrhage is one that influences the choice of therapy. If a tumor has a tendency to bleed profusely when efforts are made bronchoscopically,

genic carcinoma must be promptly differentiated from tuberculosis, since time and rest never cure a malignant growth. Waiting six weeks or longer for results of animal inoculation or tests of cultures of sputum may rob the patient of his chance of surgical cure. If on the basis of physical and x-ray examination the disease cannot be differentiated from pulmonary tuberculosis and a few specimens of sputum are negative, bronchoscopy should be performed without further delay. Inspection of the bronchi, if the patient's general condition admits it, yields valuable information that may determine not only the diagnosis but also how the case is to be managed. This is as true in pulmonary tuberculosis as it is in bronchiogenic carcinoma, since the presence or absence of endobronchial tuberculosis may alter the plans for collapse therapy. Hence, in either disease much may be gained by prompt bronchoscopic examination.

Griess, McDonald and Clagett,²⁶ in a study of the proximal extension of carcinoma of the lung in the bronchial wall, state that it is important for the surgeon to know what type of tumor he is dealing with in order to appreciate how close to the macroscopic lesion to make the operative incision. In an extremely limited number of cases it appears that on the average an adenocarcinoma extends much farther than does a squamous-cell epithelioma. With the skill of the modern bronchoscopist, biopsy can be done previous to the operation, and the surgeon, knowing what kind of lesion he is dealing with, can decide where to sever the bronchus. There are, of course, certain anatomic limits, and these probably accounted for the incision's passing through the carcinoma in some of the cases in this series. When dealing with adenocarcinomas the surgeon should, if anatomically possible, sever the bronchus more than 2 cm proximal to the gross limits of the lesion. If the tumor is a squamous-cell epithelioma, a safe distance to sever the bronchus is at least 1.5 cm.

Tinney, Moersch and McDonald²⁷ have reviewed 27 cases of neoplasm of the trachea seen at the Mayo Clinic since 1921. The lower third of the trachea is the region likeliest to be involved. Chills and fever, which frequently accompany bronchiogenic carcinoma, are less apt to occur in cases of tracheal tumor. Although routine roentgenographic studies may be of little importance in establishing the diagnosis, tomographic studies are often of considerable value. Roentgenograms taken after instillation of iodized oil into the trachea help fairly frequently to show the outlines of the lesion and often lead to the correct diagnosis. Sometimes the tumor may be seen on direct laryngoscopy. In most cases of carcinoma of the trachea, however, the diagnosis is dependent on bronchoscopic examination. The tumors in these 27 cases were divided into four distinct groups — squamous-cell carcinoma, 11 cases, cylindroma, 8 cases, adenocarcinoma, 6 cases, and hemangioendothelioma, 2 cases. Carcinoma of the

trachea offers an extremely difficult therapeutic problem, and no one form of treatment has been found satisfactory in all types of cases. Carcinoma situated in the upper portion of the trachea is best handled by means of tracheal fissure and destruction of the tumor by electrocoagulation, as advocated by Figg.²⁸ Carcinoma situated in the lower end of the trachea is best treated by electrocoagulation of the tumor through the bronchoscope. In a case of the series at the Massachusetts General Hospital in which adenocarcinoma of the trachea was extensive and could not be treated adequately by means of surgical diathermy the use of roentgen-ray therapy alone was followed by marked benefit. Although the life expectancy of most patients is between six months and one year, there are some notable exceptions. This is particularly true of tumors of the cylindroma group. One of the patients with this type of tumor died ten years after the diagnosis was made, apparently of an entirely unrelated disease. The other 7 were living and well when last heard from.

Hamartoma

McDonald, Harrington and Clagett²⁹ state that hamartoma of the lung has often been called chondroma. It is supposed to be the result of abnormal development of the bronchial anlage, — hence the name "hamartoma" (to err). The term was coined in 1904 by Albrecht, who stated

Hamartomata are tumorlike malformations in which occurs only an abnormal mixing of the normal components of the organ. The abnormality may take the form of a change in quantity, arrangement or degree of differentiation, or may comprise all three. The deduction to be drawn from histologic examination of these formations is that they have originated in an abnormal mixing of the elements or from disturbance of their development.

McDonald et al. have confined the use of the term "hamartoma of the lung" to a specific type of tumor that has a characteristic morphologic appearance, this is a solid tumor of the bronchus consisting of benign mesodermal and benign epithelial elements. Their paper is based on a study of 23 patients with hamartoma of the lung. Since the tumor is usually situated in the periphery of a pulmonary lobe, bronchoscopic examination is not of much value, but it should be done to rule out other pulmonary lesions. In 3 cases, the tumor was removed surgically, in the remaining 20, it was discovered at autopsy. These 20 cases were part of a consecutive series of 7972 cases in which autopsy was performed, the incidence of hamartoma of the lung in this series was 0.25 per cent. They conclude that this tumor occurs more frequently than has been recognized. It is strictly benign and only occasionally causes symptoms. In most cases the diagnosis has to be made by roentgenographic examination. A hamartoma should be suspected in every case of a solitary lesion of the lung. It frequently cannot be distinguished from other lesions of the lung until a

rules out tumor Exploratory thoracotomy, they conclude, is a procedure that is used too little and too late As regards safety and accuracy it is on a par with abdominal exploration

Clerf²⁰ believes that, since primary carcinoma frequently occurs in large bronchi that are accessible to bronchoscopic investigation, much aid has been given to the clinician by the bronchologist in its diagnosis There is no question in diagnosis if the classic infiltrating, ulcerated lesion is observed and a biopsy specimen can be secured Lesions occurring in an upper lobe "around the corner" or in subdivisions of the lower lobes or middle lobe present difficulties that must be promptly surmounted if any benefit is to be gained by establishing a positive early diagnosis Although the orifices of the upper lobe can be satisfactorily inspected by a telescopic obturator introduced through the bronchoscope, too often the lesion is beyond this point In these cases it is desirable to use a flexible, tipped aspirating tube attached to a collector so that secretions can be secured from "around the corner" and examined for neoplastic cells Careful attention to this will be rewarded by a fairly large number of positive findings A similar procedure can be instituted for subdivisions of the bronchi of the middle and the lower lobe The bronchologist also should observe whether there is narrowing, deformation, fixation or rigidity of a bronchus owing to neoplastic infiltration In the absence of biopsy material these findings are of great diagnostic significance Information concerning the mobility of the carina and the angle of division of the trachea is of importance to the thoracic surgeon

Miranda and Gonnella²¹ report a case of primary bronchial carcinoma with early cutaneous metastasis This is a rare site for metastatic lesions from bronchial carcinoma The patient was a man of thirty-seven who one month after recovery from pneumonia developed a chronic bronchitis with multiple cutaneous nodules over the chest wall A diagnosis of bronchial cancer was confirmed by bronchoscopy and by biopsy of the metastatic nodules

In a paper on the difficulties encountered in the differential diagnosis of bronchiogenic carcinoma, Bloch, Adams, Thorton and Bryant²² note the increased interest in carcinoma of the lung, which has led to much improvement in the diagnosis of pulmonary tumors With an ever better roentgen technic and by bronchoscopy, their differentiation from other involvements of the lungs seems to have become comparatively easy, and a diminishing number of patients with endobronchial cancer die because of an erroneous diagnosis Routine chest fluoroscopy in 15,000 patients showed that 91 (0.6 per cent) had intrathoracic neoplasms X-ray examination, which is indispensable for the discovery of a lesion, in no case offers a reliable differential diagnosis Although the bronchoscope is also indispensable, bronchoscopy also results in failure

to make a positive diagnosis when the tumor is inaccessible to the bronchoscope Bronchoscopy in early peripheral tumors, which according to Jaffe²³ constitute 13 per cent of the total incidence, is always negative In the absence of bronchoscopic findings, therefore, surgical exploration alone can lead to an acceptable diagnosis It should be undertaken even in early cases when there seems to be a strong enough possibility of neoplasm

In an analysis of 175 proved cases of bronchiogenic carcinoma, Holinger, Hara and Hirsch²⁴ have called attention to the United States Government's vital statistics on carcinoma in children and young adults In 1940, 1 death occurred in an infant under one year of age, 3 in those under two years, 2 in those under four years, 8 in children between five and nine years, 18 in those between ten and eighteen, 22 in those between fifteen and nineteen, 44 in persons between twenty and twenty-four and 38 in those between twenty-five and twenty-nine The disease is much more frequent on the right side than on the left, the ratio being 11.6 Bronchoscopic examination should be made in patients with obscure pulmonary disease as suggested by the history, symptomatology and x-ray findings Such symptoms as persistent cough, wheeze, unexplained hemoptysis and recurring or so-called "unresolved" pneumonia are all specific indications for bronchoscopy All too frequently, however, such indications are ignored and this examination is postponed or not considered The presumptive diagnosis of atypical pneumonia and the prolonged ineffective use of chemotherapy in an effort to clear a supposed pneumonia have been responsible for many delays in bronchoscopic examination In this series, six months or longer elapsed between the initial symptoms and bronchoscopy in 86 (50 per cent) of the patients In 14 (8 per cent) more than one year elapsed Among the latter group were 3 who had had a cough for more than ten years and could not accurately tell when their illness began The treatment of bronchiogenic carcinoma is primarily surgical Bronchoscopic treatment of bronchiogenic carcinoma is mentioned not as opposed to surgery but as a means of therapy in patients otherwise inoperable Although the results of endobronchial therapy by implantation of radon seeds or radium directly into the tumor have usually been palliative, clinical cures by the use of this method together with surgical diathermy have been reported

Pillsbury and Wassersug²⁵ have studied 12 proved cases of bronchiogenic carcinoma that were admitted to a tuberculosis hospital Patients with bronchiogenic carcinoma are occasionally admitted to a sanatorium, either for observation for tuberculosis or because a definite diagnosis of tuberculosis has already been made Since the clinical findings may be misleading, reliance must be placed on other diagnostic aids, such as x-ray examination, bronchoscopy and exploratory thoracotomy Bronchio-

genic carcinoma must be promptly differentiated from tuberculosis, since time and rest never cure a malignant growth. Waiting six weeks or longer for results of animal inoculation or tests of cultures of sputum may rob the patient of his chance of surgical cure. If on the basis of physical and x-ray examination the disease cannot be differentiated from pulmonary tuberculosis and a few specimens of sputum are negative, bronchoscopy should be performed without further delay. Inspection of the bronchi, if the patient's general condition admits it, yields valuable information that may determine not only the diagnosis but also how the case is to be managed. This is as true in pulmonary tuberculosis as it is in bronchiogenic carcinoma, since the presence or absence of endobronchial tuberculosis may alter the plans for collapse therapy. Hence, in either disease much may be gained by prompt bronchoscopic examination.

Griess, McDonald and Clagett,²⁶ in a study of the proximal extension of carcinoma of the lung in the bronchial wall, state that it is important for the surgeon to know what type of tumor he is dealing with in order to appreciate how close to the macroscopic lesion to make the operative incision. In an extremely limited number of cases it appears that on the average an adenocarcinoma extends much farther than does a squamous-cell epithelioma. With the skill of the modern bronchoscopist, biopsy can be done previous to the operation, and the surgeon, knowing what kind of lesion he is dealing with, can decide where to sever the bronchus. There are, of course, certain anatomic limits, and these probably accounted for the incision's passing through the carcinoma in some of the cases in this series. When dealing with adenocarcinomas the surgeon should, if anatomically possible, sever the bronchus more than 2 cm proximal to the gross limits of the lesion. If the tumor is a squamous-cell epithelioma, a safe distance to sever the bronchus is at least 1.5 cm.

Tinney, Moersch and McDonald²⁷ have reviewed 27 cases of neoplasm of the trachea seen at the Mayo Clinic since 1921. The lower third of the trachea is the region likeliest to be involved. Chills and fever, which frequently accompany bronchiogenic carcinoma, are less apt to occur in cases of tracheal tumor. Although routine roentgenographic studies may be of little importance in establishing the diagnosis, tomographic studies are often of considerable value. Roentgenograms taken after instillation of iodized oil into the trachea help fairly frequently to show the outlines of the lesion and often lead to the correct diagnosis. Sometimes the tumor may be seen on direct laryngoscopy. In most cases of carcinoma of the trachea, however, the diagnosis is dependent on bronchoscopic examination. The tumors in these 27 cases were divided into four distinct groups — squamous-cell carcinoma, 11 cases, cylindroma, 8 cases, adenocarcinoma, 6 cases, and hemangioendothelioma, 2 cases. Carcinoma of the

trachea offers an extremely difficult therapeutic problem, and no one form of treatment has been found satisfactory in all types of cases. Carcinoma situated in the upper portion of the trachea is best handled by means of tracheal fissure and destruction of the tumor by electrocoagulation, as advocated by Figi.²⁸ Carcinoma situated in the lower end of the trachea is best treated by electrocoagulation of the tumor through the bronchoscope. In a case of the series at the Massachusetts General Hospital in which adenocarcinoma of the trachea was extensive and could not be treated adequately by means of surgical diathermy the use of roentgen-ray therapy alone was followed by marked benefit. Although the life expectancy of most patients is between six months and one year, there are some notable exceptions. This is particularly true of tumors of the cylindroma group. One of the patients with this type of tumor died ten years after the diagnosis was made, apparently of an entirely unrelated disease. The other 7 were living and well when last heard from.

Hamartoma

McDonald, Harrington and Clagett²⁹ state that hamartoma of the lung has often been called chondroma. It is supposed to be the result of abnormal development of the bronchial anlage, — hence the name "hamartoma" (to err). The term was coined in 1904 by Albrecht, who stated

Hamartomata are tumorlike malformations in which occurs only an abnormal mixing of the normal components of the organ. The abnormality may take the form of a change in quantity, arrangement or degree of differentiation, or may comprise all three. The deduction to be drawn from histologic examination of these formations is that they have originated in an abnormal mixing of the elements or from disturbance of their development.

McDonald et al. have confined the use of the term "hamartoma of the lung" to a specific type of tumor that has a characteristic morphologic appearance, this is a solid tumor of the bronchus consisting of benign mesodermal and benign epithelial elements. Their paper is based on a study of 23 patients with hamartoma of the lung. Since the tumor is usually situated in the periphery of a pulmonary lobe, bronchoscopic examination is not of much value, but it should be done to rule out other pulmonary lesions. In 3 cases, the tumor was removed surgically, in the remaining 20, it was discovered at autopsy. These 20 cases were part of a consecutive series of 7972 cases in which autopsy was performed, the incidence of hamartoma of the lung in this series was 0.25 per cent. They conclude that this tumor occurs more frequently than has been recognized. It is strictly benign and only occasionally causes symptoms. In most cases the diagnosis has to be made by roentgenographic examination. A hamartoma should be suspected in every case of a solitary lesion of the lung. It frequently cannot be distinguished from other lesions of the lung until a

specimen of the tumor is examined microscopically. Treatment consists of excision of the tumor. One should try to conserve as much pulmonary tissue as possible.

Tuberculosis

Clerf²⁰ believes that credit must be given to bronchoscopy for the discovery that certain signs and symptoms in tuberculous patients and certain complications following the surgical treatment of tuberculosis are the result of tuberculous involvement of the larger bronchi by infiltrative, ulcerogranulomatous or cicatricial lesions. It is in this group that bronchoscopy plays a definite part in diagnosis as well as in treatment. Inspection of the tracheobronchial tree is usually adequate to determine the presence of infiltrative and ulcerogranulomatous lesions, and biopsy is therefore advised against unless there is considerable evidence to support the belief that carcinoma is present. It is important to discover the presence of obstructive lesions in a bronchus so that the clinician or surgeon may take this into account when contemplating some form of collapse therapy.

Wilson³⁰ has attempted to correlate the clinical and pathological findings in tracheobronchial tuberculosis. Endobronchial tuberculosis has been found in 10 to 15 per cent of patients at the time of sanatorium admission. The author advises that no attempt be made to dilate fibrotic stenosis; instead, he suggests thoracoplasty or pneumonectomy. He opposes biopsy because of the possibility of initiating ulceration. He advises treatment with silver nitrate every two weeks until healing ensues, following which the intervals between applications should be gradually lengthened. If no response is obtained over a reasonable time, pulmonary resection is advised.

Chamberlain,³¹ in a discussion of lobectomy versus thoracoplasty in the treatment of tuberculosis, repeatedly states that endobronchial tuberculosis is present in all cases of tuberculosis with cavitation. Although clinically physicians have been aware of endobronchial tuberculosis only in the last ten years, it has always been present, though it may have been beneath the mucosa or just beyond the view of the bronchoscopist. The significance of this complication is directly proportional to the kind of endobronchial lesion, the size of the bronchus involved and the degree of obstruction. Obviously, a small submucous tubercle is not so serious as an ulcerative lesion that circumscribes and almost completely obstructs a large bronchus. An ulcerative endobronchial lesion of moderate or extreme severity implies severe damage distal to it in the form of obstructive emphysema, suppuration, atelectasis or tension cavities. A definitive form of therapy is therefore indicated if one or more of these complications exist. Thoracoplasty had met with considerable success before physicians were aware of the

presence of endobronchial tuberculosis, and they now intentionally do thoracoplasties in cases with certain types of lesions in the major bronchi (visible at bronchoscopy), with good results as reported by Alexander, Tuttle, Chamberlain, and Gordon.³² It must also be kept in mind that in every case of tuberculosis there are both obstructive (endobronchial disease) and overdistention types of emphysema, which are directly proportional to the amount and duration of the tuberculosis. Endobronchial tuberculosis is present in all cases with cavitation, and its significance is essentially dependent on the degree of bronchial obstruction, which may cause obstructive emphysema, suppuration, atelectasis and tension cavities. Thoracoplasty is successful in 75 per cent of the cases in which the diseased bronchus is visible by bronchoscopy.

In a discussion of pulmonary resection in the treatment of tuberculosis, Overholt and Wilson³³ point out that bronchoscopy has revealed the presence of bronchial tuberculosis in many patients. This has helped to avoid many of the mistakes made in the earlier selection of cases and to plan the proper operation and the extent of resection. Tuberculous bronchitis, either active or inactive, is not itself a contraindication to resection even if it has to be traversed during the procedure. On the contrary, this complication is often an indication for resection.

Stone,³⁴ in a discussion of the clinical aspects of endobronchial tuberculosis, states that the lung specialist can never consider himself adequately trained until he has mastered the art of bronchoscopy. Furthermore, bronchoscopy will never render its maximum service to medicine until it is embraced by the man to whom it rightfully belongs—the specialist in chest diseases. The incidence of endobronchial tuberculosis obviously varies with the zeal as well as with the skill of the operator. The diagnosis of endobronchial tuberculosis can be definitely made only when it can be visualized by the bronchoscopist. The chief symptoms in this group are a localized wheeze and loud auscultatory rhonchi. Next to wheezing and rhonchi is the completely collapsed lung or the so-called “opaque” unexpandable lung.

Postoperative Use of the Bronchoscope

Clerf³⁰ points out that an extremely simple method of removing excessive secretions in the tracheobronchial tree after an operation consists of the employment of a catheter introduced into the trachea and attached to a mechanical apparatus. Patients who cannot be relieved by these simple methods should be aspirated by bronchoscopy.

Aronovitch³⁵ calls attention to the formation of a mucous plug following operation, with the familiar picture of fever, shallow respirations, cyanosis and chest pain. Sometimes exceedingly simple procedures such as a slap on the back, directing the patient to cough hard or placing him in the proper

position dislodge the plug. If after twenty-four hours these measures fail when used in combination with adrenalin or ephedrine, aspiration should be performed.

Lundy and his associates³⁶ in a report on anesthesiology have again emphasized the importance of bronchoscopic aspiration at the end of operation. Such an operation is generally acknowledged to be valuable and has proved to be so in their hands, especially in intrapulmonary operations.

In the surgical treatment of bronchiectasis, Clagett³⁷ uses bronchoscopy immediately after operation to clear the bronchial tree.

Lung Abscess

According to Clerf,²⁰ in the earlier days of bronchoscopy before much progress had been made in the successful treatment of pulmonary abscess by thoracic surgery, it was not unusual to practice bronchoscopic aspiration in these cases. The fundamental principle was a sound one — namely, that the abscess would undergo resolution if adequate drainage of pus could be established and maintained. In a certain number of cases of acute pulmonary abscess one can obtain satisfactory results if drainage can be improved by bronchoscopic aspiration with curved, flexible, tipped aspirating tubes and the employment of shrinking solutions. It is believed inadvisable, however, to continue bronchoscopic treatment for more than two or three weeks unless continuous improvement is observed. If the temperature does not promptly return to normal after several aspirations and definite improvement is not shown by roentgen-ray examination, bronchoscopic treatment should be discontinued.

No report can be given on the newer drugs, notably sulfonamides and penicillin employed bronchoscopically. It is believed that these exert little effect if introduced into the abscess cavity through the bronchoscope. In chronic abscess and in cases in which there is a question of new growth complicated by abscess, a diagnostic bronchoscopy is indicated. Cases of endobronchial foreign body, either exogenous or endogenous, complicated by pulmonary abscess have been recorded, and a number of cases of unsuspected carcinoma of the bronchus have been treated surgically as cases of pulmonary abscess, with unfavorable results.

Smyth and Billingslea,³⁸ in a review of the literature, have found reference to 31 cases of lung abscess treated with penicillin. Thirteen have shown complete recovery, 8 have shown satisfactory improvement, and in 10 cases there was either no change or death occurred. In a study of 4 of their own cases, these authors state that the long-continued use of penicillin has resulted in the control of the surrounding pneumonitis in all 4 cases and has permitted the healing of the abscess cavities in 3 of them. They are of the opinion that if lung abscesses are recognized early and are vigorously

treated by long-continued penicillin administration, there will be an appreciable reduction in the morbidity and mortality from this disease.

Valle³⁹ has analyzed 244 cases of lung abscess. The differentiation of simple lung abscess and carcinoma is difficult because there is often a combination of the two resulting from an infection of the carcinoma. The x-ray picture of bronchiogenic carcinoma often shows atelectasis of one lobe and a poorly outlined shadow. Some cases of carcinoma develop pleural fluid in which carcinoma cells can be detected. The author believes that the best means of differentiating the two is bronchoscopy, which in bronchiogenic carcinoma generally reveals the growth to be blocking the bronchus, from which a biopsy can be taken. Sometimes the bronchus can be seen to be compressed from without. In a few cases the tumor is out of reach of the bronchoscope and an accurate diagnosis cannot be made until an exploratory thoracotomy has been performed. As regards etiology and pathogenesis, Valle found that lung abscesses developed in 41 cases after tonsillectomy under anesthesia and in 27 after abdominal operation under general anesthesia. In this connection he states that Myerson subjected to bronchoscopy a number of patients who had had tonsillectomies performed under general and local anesthesia and found blood and mucus in the lower bronchi in 90 per cent of the cases with general anesthesia, but in a much lower percentage among those having local anesthesia and the cough reflex present. Valle and his associates consider bronchoscopy one of the most important features in the diagnosis and treatment of lung abscess. Of 80 patients treated by bronchoscopy alone, 47 were improved. As a diagnostic procedure it is extremely useful in localization of the abscess by revealing which bronchus is the source of pus. As a part of the treatment bronchoscopy is much used. Sometimes the draining bronchus becomes plugged, and by introducing the flexible suction tip into the bronchus the mucous plug is removed and drainage promoted. Patients who are confined to bed can often be so greatly improved by several bronchoscopic aspirations that the later surgical drainage becomes less hazardous. Valle considers bronchoscopy imperative whenever aspiration of a foreign body into the bronchial tree is suspected.

Sweet⁴⁰ has analyzed the cases of lung abscess from 1938 to 1942 at the Massachusetts General Hospital. He notes the significant fact that the total duration of the disease in many of the spontaneous-cure group was of surprising length. Although 9 patients recovered in three months or less, the disease lasted for three to six months in 8 cases and from six to twelve months in 6. Two patients recovered after the expiration of one year. The use of sulfonamide chemotherapy produced no material change in the results in this series. Although lung abscess continues to be a serious disease, there

has occurred over the last ten or more years an encouraging increase in the number of cures and a gratifying reduction in the mortality rate

Hemoptysis

Adams and Ficarra⁴¹ note that "hemoptysis" is a term specifically applied to bronchopulmonary hemorrhage. Before bleeding emanating from the nose or mouth can be definitely called hemoptysis, all forms of pseudohemoptysis must be eliminated. The types of bleeding most frequently confused with hemoptysis are hematemeses and epistaxis. Inspection of the nasal and oral pharynx will exclude epistaxis and bleeding from the pharynx, the back of the nose, the tonsils, teeth, gums, tongue and mucous membrane of the buccal cavity. The differential diagnosis between hemorrhage from the alimentary canal and bronchopulmonary hemorrhage is often difficult. The majority of causes for hemoptysis can be classified in the following groups: tuberculosis of the lung and bronchi, bronchiectasis, abscess of the lung, lobar pneumonia, infarction of the lung, carcinoma of the lung, traumatic lesions of the chest and congestive heart failure. Less frequent etiologic agents are chronic bronchitis, diseases of the larynx, adenoma of the bronchus, gangrene of the lung and mediastinal tumors. The diagnosis can be made from the history and physical findings, roentgen-ray studies, bronchoscopy and laboratory data, including sputum studies. Bronchoscopy as a therapeutic measure is useful when bleeding has been so extensive as to cause bronchial obstruction or atelectasis.

Complications

Abbott and De Oliveira⁴² have reported 4 cases of pneumothorax occurring in conjunction with bronchoscopy and 1 case coincident to esophagoscopy. In the cases reported no major bronchi suffered direct injury. They describe the phenomenon not as a complication of bronchoscopy but rather as an indirect hazard of the coughing paroxysm subsequent to endoscopic manipulation.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32271

PRESENTATION OF CASE

A sixteen-year-old schoolgirl entered the hospital because of headache, photophobia, diplopia and mild tinnitus.

Thirty days before admission, during a lecture, the patient had a sudden frontal headache, which was the first severe headache she had ever had. Subsequently there were severe headaches lasting about five minutes each, with intervals of from five to ten minutes between them. The pain started in the forehead and radiated down the neck, shoulders and arms. Each attack was accompanied by a generalized sensation of warmth. A dull constant ache gradually developed between attacks. Twenty days before admission, glasses were prescribed. Four days later the patient noticed blurring of vision, and on the following day she felt nauseated and at the same time began to have double vision. On the next day there was an episode of vomiting, the only one during this illness. One week before admission she felt dizzy and unsteady on standing. Buzzing in the ears, excessive lacrimation and photophobia developed in the last four days.

On physical examination the patient was alert and oriented. The pupils were equal and measured 4 mm. They did not react to light but did react to convergence. There was a 15° limitation of abduction of the left eye. The diplopia disappeared when the patient looked 10° to the right. There was limitation of upward gaze, with the left eye elevating 10 to 15° better than the right. On extreme supraversion there was a strong, sudden convergence. The visual fields were normal. There was papilledema of 1 or 2 diopters on the right and 2 or 3 diopters on the left. There was slight vertigo. Flexion of the neck was moderately limited and painful. There was a positive Kernig sign. The tendon, abdominal and plantar reflexes were normal. Sensation was normal.

The temperature was 99°F, the pulse 82, and the respirations 22. The blood pressure was 115 systolic, 75 diastolic.

There were 14.5 gm of hemoglobin per 100 cc of blood. The white-cell count was 10,300, with 72 per cent neutrophils. The urine had a specific gravity of 1.021. There was a + test for albumin, and the sediment contained 20 white cells and a rare red cell per high-power field. The spinal fluid was under an initial pressure equivalent to 260 mm of water, which fell to 150 mm with removal of 10 cc. The fluid was clear and contained 124 red cells, 6 lymphocytes and 1 polymorphonuclear cell per cubic millimeter. The total protein was 36 mg per 100 cc. The electroencephalogram was moderately abnormal, with suspicious activity on the left side that was thought to be slightly more marked toward the occiput, although a positive localization was not possible. X-ray examination of the skull was negative. The blood and spinal-fluid Hinton and Wassermann tests were negative.

On the fourth hospital day bilateral occipital burr holes were made. Immediately after operation, the patient was restless, had a severe headache and did not recognize people. Four hours later she suddenly stopped breathing.

DIFFERENTIAL DIAGNOSIS

DR. DAVID COGAN: As I read over this record, it seemed to me to include a number of red herrings, and I should like to go over it sequentially and analyze the symptoms and findings, eliminating the insignificant ones.

In the first place, we are told that this patient, a sixteen-year-old girl, had sudden spontaneous headache. In itself, that symptom suggests a rupture of a congenital aneurysm. Ordinarily aneurysm produces headaches that have a sudden onset, but I have seen patients in whom the recurrences took place at reasonably long intervals—a matter of days, not every five or ten minutes as in this case.

Casting about for other causes of intermittent severe headache, one must think of intermittent block of the aqueduct—something in the region of the anterior midbrain. In that connection it would be interesting to know if movements of the head precipitated the headache or relieved the headache, as it sometimes does when there is a ball-valve obstruction of the aqueduct.

The pain started in the forehead and radiated down the neck, shoulders and arms, all of which suggests nothing to me. The generalized sensation of warmth with the attacks is of interest. If there were other corroborative evidence, such a sensation would be suggestive of a diencephalic lesion. The rest of the history, including a note about vomiting and dizziness, is compatible with increased intracranial pressure, all of which, except for the photophobia, I do not know how to interpret.

Physical examination disclosed something definite: the pupils were equal, measured 4 mm and did not react to light but did react to convergence. These

were not Argyll-Robertson pupils because of their size. A pupil of 4 mm is normal for a sixteen-year-old person. If the pupils were typically Argyll-Robertson, they would be miotic, and if large they would be of unequal size and irregular. These

give weakness of the external rectus muscle, presumably through involvement of the sixth nerve as it angulates over the sphenoidal ridge.

Limitation of upward gaze is significant and goes with the type of pupils that she had, under the

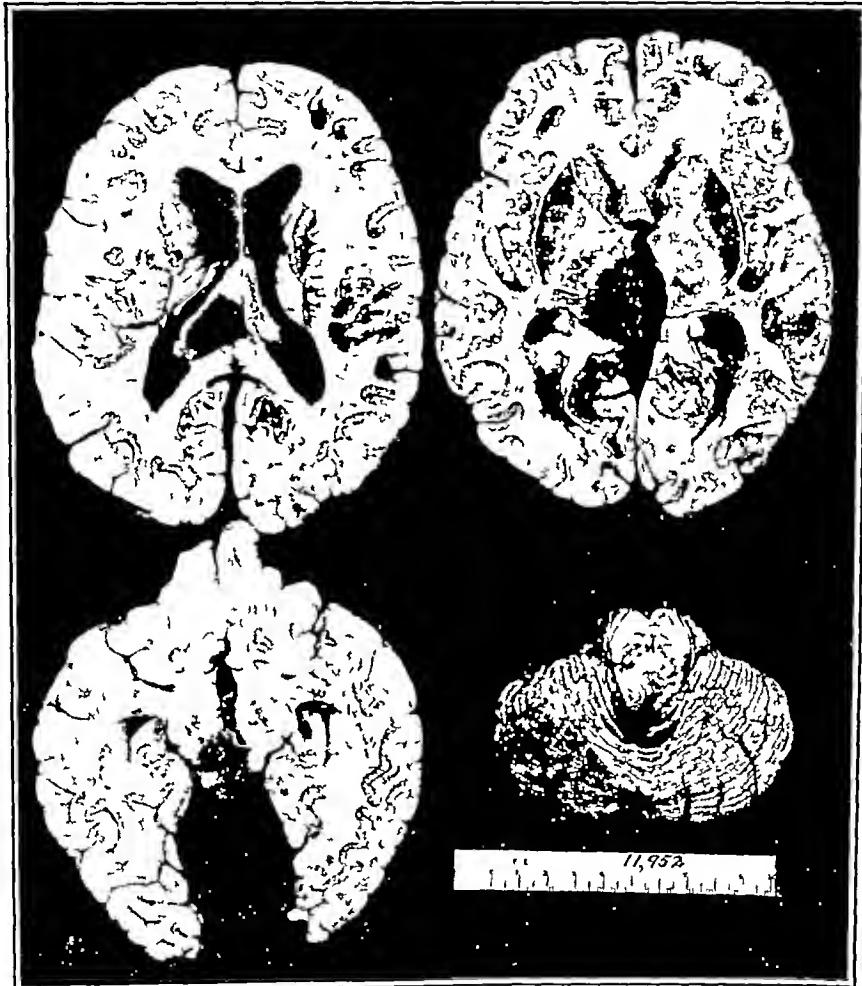


FIGURE 1

normal-sized pupils, which reacted for near vision but not for light, are strongly indicative of a lesion in the region of the superior colliculus.

There was a 15° limitation of abduction of the left eye, which I assume was due to paralysis of the external rectus muscle, since we are told that diplopia disappeared when the patient looked 10° to the right. But in the presence of increased intracranial pressure an altered paralysis of the rectus means nothing so far as localization is concerned. Increased intracranial pressure alone can

heading of Parinaud's syndrome, which is pathognomonic of a lesion in the region of the superior colliculus. The paralysis of upward gaze and the pupillary signs fit into the syndrome. The statement that the left eye elevated 10 to 15° better than the right is confusing to me, especially since the diplopia disappeared when the patient looked just 10° to the right. If the left eye showed a difference of 15° somewhat above the midline, I should expect vertical diplopia in the horizontal position.

I am going to have the temerity to say that I think that observation may have been erroneous

On extreme supraversion there was strong sudden convergence. That means on attempted extreme supraversion, because the patient had weakness of upward gaze. Sudden convergence is a reaction that occurs in people who attempt to do something that they cannot do. This patient attempted in vain to look up, and convergence is not an infrequent reaction under those circumstances and has no localizing significance.

The papilledema goes with increased intracranial pressure, which is also compatible with a lesion in the region of the superior colliculus obstructing the aqueduct. The slight vertigo, the flexion of the neck and the positive Kernig sign, I interpret as resulting from the increased intracranial pressure and as having no further significance. There was no evidence of meningitis or of tumor of the posterior fossa, which might cause these signs.

The neurologic examination was negative except for the eyes. The laboratory data are not helpful. The urine was not a catheterized specimen, and I assume that it was not significant. I was surprised that a lumbar puncture was done, in view of the apparent increased intracranial pressure, which was evident in the papilledema. The fluid was clear and contained 131 cells per cubic millimeter. I have been looking for other evidence of aneurysm, but in view of the fact that this fluid was not xanthochromic and the protein was normal, I shall interpret the cells as being incidental to the puncture. The electroencephalogram I take to be equivocal.

In summary, I believe that the signs point to a lesion in the region of the superior colliculus with increased intracranial pressure and no definite indication of the nature of the lesion, but in view of the increased intracranial pressure I think that the likeliest diagnosis is a tumor. The most frequent tumors of this region are pinealoma, teratoma of the pineal body, tuberculoma and glioma of the mesencephalon. In the cases that I have seen with this general syndrome, however, there were two patients with aneurysm who never came to autopsy, so that I do not know where the aneurysm was. But I am humbled in the suggestion that it was a tumor by the fact that there were these cases of aneurysm.

We are told that occipital burr holes were made, I am at a loss to understand why, since there was no evidence of subdural hematoma, and I am wondering if the burr holes were made preliminary to an air injection and why the results of this injection were not described. Certainly air injection in this case would have been most helpful, particularly air in the region of the third ventricle.

DR CHARLES S KUBIK: The lateral ventricles were tapped, but no air was put into them.

DR COGAN: Death I assume to have been caused by a pressure cone. At least one other patient seen

in this hospital four or five years ago with a pinealoma met death in a similar fashion from a pressure cone.

CLINICAL DIAGNOSIS

Midbrain tumor

DR COGAN'S DIAGNOSES

Lesion in the region of the superior colliculi (probably tumor, possibly aneurysm)

Pressure cone as cause of death

ANATOMICAL DIAGNOSIS

Pinealoma.

PATHOLOGICAL DISCUSSION

DR KUBIK: In the region between the quadrigeminal plate and the splenium of the corpus callosum, where the pineal gland would normally be situated, there was a soft, friable tumor mass, 2.5 cm

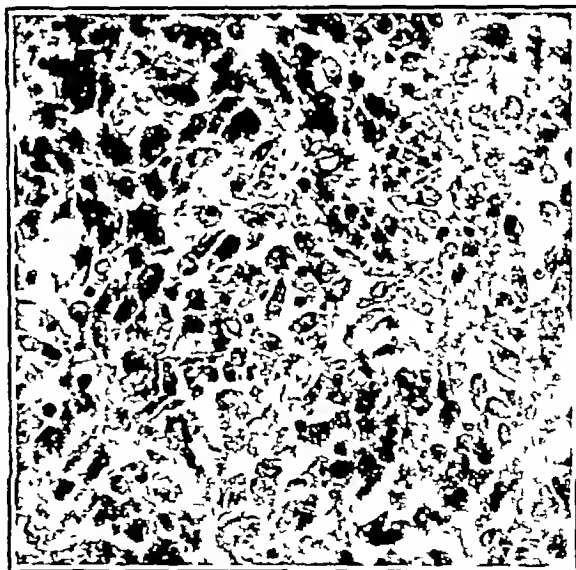


FIGURE 2

to 3.0 cm in diameter, which extended forward into the third ventricle. In this position it was situated between and invaded the posterior portions of the optic thalami. It also extended downward, invading the superior and inferior colliculi and the upper part of the tegmen of the pons. The aqueduct was partly occluded, and as a result the lateral ventricles were enlarged to three or four times their normal size (Fig 1).

In cases of increased intracranial pressure in which death results from respiratory failure, a cerebellar

pressure cone is usually found at autopsy. The lower poles of the cerebellum and the medulla are forced downward into the foramen magnum, the herniated portions of the cerebellum forming a wedge that compresses the medulla and obliterates the blood supply of the respiratory center. In this case there was no pressure cone. It is possible, I suppose, that a high and rapid rise in intracranial pressure produces a similar effect on the respiratory center and results in death before any appreciable herniation of the cerebellum has taken place.

The tumor was composed of medium-sized, rounded and polyhedral pyramidal cells, some of which had well defined short cytoplasmic processes (Fig 2). They bore a close resemblance to cells of the normal pineal gland. Scattered among the tumor cells were a few lymphocytes. In this respect the tumor differed from some of the other pinealomas examined here, in which there were large numbers of lymphocytes and plasma cells, not only in the tumor but also in the adjacent subarachnoid and perivascular spaces.

CASE 32272

PRESENTATION OF CASE

A thirty-three-year-old married woman, a factory employee, entered the hospital because of intermittent fever.

Two years and eight months before admission the patient started working in a war plant. She was not exposed to any toxic substances. Six months later she began to have frequent colds and bouts of hoarseness. On one occasion she had a severe sore throat, with a temperature of 104°F lasting for several days. During the succeeding six months she lost weight, had a poor appetite, and a dry hacking cough and worked only part time. She began to run an intermittent fever of 101 to 102°F. At that time a chest film was taken, and blood tests were performed, she did not know the results. All her teeth were removed. In the two years preceding admission she was constantly fatigued and had frequent chills and fever, usually accompanied by sweats at night. She lost 60 pounds. Her condition was studied at a community hospital for five days, but no diagnosis was made. While in the hospital she developed a boil on the buttock, which was lanced. At home she had three more boils, which ruptured and drained spontaneously. During the two months before admission a dull ache developed along the left costal margin in the midaxillary line. There was a sharp pain on coughing, with occasional vomiting after coughing. With the appearance of the ache, the temperature rose to 104°F and remained elevated. Violent chills developed, and were accompanied by throbbing frontal headaches. During the chills the hands became white, and the fingertips blue. She fainted twice. During this illness, the menstrual

periods gradually shortened to one day, and the flow was scanty. There were no other past illnesses. A former landlady with whom the patient had lived for two years had had cancer and possibly tuberculosis.

Fifteen and thirteen years prior to admission the patient underwent cesarean sections because of pelvic deformity from an automobile accident in childhood. The right ovary was removed at the second operation. Following this procedure a large abscess developed in the wound, taking four months to heal. Six years before admission she had an episode of severe lower abdominal pain and a vaginal discharge lasting four days.

On physical examination the patient was flushed and feverish. The heart sounds were forceful. There was a Grade II apical systolic murmur transmitted to the axilla and a Grade II pulmonic systolic murmur. The pulmonic second sound was greater than the aortic. Breath sounds, fremitus and voice sounds were absent over the entire left chest below the level of the eighth thoracic vertebra. The left diaphragm did not move. The whole area was tender. The left side of the abdomen was tender, with marked sensitivity in the upper quadrant. A mass in this region seemed to move on inspiration and was exquisitely tender. There was considerable voluntary spasm. The left vaginal vault was tender.

Examination of the blood showed a red-cell count of 3,100,000, with a hemoglobin of 8.5 gm. The white-cell count was 20,500 with 94 per cent neutrophils and a marked shift to the left. The urine had a specific gravity of 1.003. There was a ++ test for albumin. The sediment contained 200 to 400 white cells in clumps per high-power field.

X-ray examination showed the right side of the chest to be normal. The left leaf of the diaphragm was elevated and limited in motion. There were linear areas of atelectasis above the diaphragm. The heart was normal. A large tumor mass in the left upper quadrant, measuring approximately 10 by 14 cm in diameter, seemed to occupy the site of the left kidney. The corrected sedimentation rate was 13 mm per minute. The tuberculin test was positive in a dilution of 1:100,000. A phenol-sulfonephthalein test showed 85 per cent excretion of the dye in two hours. No dye was excreted by the left kidney after intravenous pyelography. Abundant beta-hemolytic streptococci were cultured from the urine. The blood culture was negative. Serum agglutination tests for the typhoid-paratyphoid group of organisms and for *Brucella* were negative. An electrocardiogram was normal.

An operation was performed on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR WYLAND F. LEADBETTER. We are dealing with the illness of a thirty-three-year-old woman,

which presumably began about two years before admission to the hospital. The illness was characterized by intermittent attacks of chills and fever, as well as loss of weight and appetite, and was punctuated by at least one episode of severe sore throat, with a temperature of 104°F. At one time all her teeth were removed, presumably following search for foci of infection. She developed a series of boils, which probably have no bearing on the subsequent course of the case, although this fact should be kept in mind. She was admitted to a hospital for five days during a period when she was having chills and fever, but no explanation for the symptoms was found. She had at times had a dry cough, not a productive cough, if one can trust the history. Two months before admission to this hospital she had localizing signs for the first time. She began to develop pain and discomfort in the left upper abdomen and left flank, and reported the development of a persistent temperature, which was stated to have reached 104°F and to have remained at that level. On admission to the hospital she was obviously very sick. There was absence of breath sounds in the left chest below the eighth rib. There was tenderness in the left upper abdomen and flank, and an obvious mass could be felt in this area. She had a rather marked secondary anemia, and a white-cell count of 20,500, with 94 per cent neutrophils. The urine showed a specific gravity of 1.003, which I think is of no significance, because we do not know under what conditions it was obtained. There was a ++ test for albumin, and the urinary sediment showed 200 to 400 white cells per high-power field — in other words, there was a marked pyuria.

An x-ray film showed a clear right chest, an elevation of the diaphragm on the left, with limitation of motion, and evidence of atelectasis in the left lower lung, presumably due to pressure from the mass below the diaphragm. A plain x-ray film of the abdomen is said to have shown a large tumor mass measuring 10 by 14 cm. I should think that that was not an unusually large tumor mass, particularly if it was associated with the kidney. A tuberculin test was positive in a dilution of 1:100,000. A phenolsulfonephthalein test showed 85 per cent excretion in two hours, which I presume was considered normal. An intravenous pyelogram showed no dye coming through the left kidney. I think that we can assume that the right kidney was normal. Interestingly enough, abundant beta-hemolytic streptococci were cultured from the urine. Although such a finding is not rare, it is difficult to explain this woman's symptoms on such a basis. A blood culture was negative. I assume that the question of subacute bacterial endocarditis came up. The negative culture may be considered to rule it out. Agglutination tests for typhoid, paratyphoid and brucellar organisms were negative. The electrocardiogram was normal.

On physical examination the patient had evidence of systolic apical and pulmonic murmurs. In view of the long illness and secondary anemia, I assume that those could be considered to be benign murmurs and that increased intrapulmonic pressure might have caused accentuation of the pulmonic second sound.

Before we go any farther I think that it would be of interest to see the x-ray films. It should be quite simple to arrive at a definite diagnosis in this case, provided that there is a good pyelogram. We can assume that the difficulties of this patient were localized in the left kidney because of the mass in that region, the fever, the elevated white-cell count, the pyuria and the nonfunctioning left kidney.

DR JAMES R. LINGLEY: This film shows the high left diaphragm. The density in the lower lung field is, I think, quite consistent with atelectasis. This plain film of the abdomen shows a large mass on the left side, which has the shape of the kidney, and on the intravenous pyelogram there is evidence of excretion on the right side and the pelvis and calyces on that side are somewhat elongated. On the left side there is no evidence of excretion.

DR LEADBETTER: There is no evidence of a perinephric mass?

DR LINGLEY: No.

DR LEADBETTER: A retrograde pyelogram of the left kidney would have been helpful, because there are a good many possibilities. I think that it is impossible to arrive at a specific diagnosis other than to assume that the patient had an enlarged left kidney, pyuria, with an elevated temperature, and presumably pyonephrosis. This was a long-standing illness, and if we assume that the illness over a period of two years was due to infection in the left kidney, extension to the perinephric tissues or the development of an actual perinephric abscess would not be unusual at this late date. However, I think that the x-ray film does not suggest any evidence of a perinephric abscess, and we are forced to assume that she had a pyonephrosis and preceding that a pyelonephritis that was active at intervals, at least over a two-year period. The possibility of a carbuncle of the kidney should be mentioned, I suppose, but I should stress the fact, if the culture report is to be trusted, that beta-hemolytic streptococci would probably not cause an abscess so frequently as staphylococci, and I believe that this woman probably did not have a carbuncle of the kidney or a perinephric abscess.

Assuming that the woman did have a pyonephrosis, one must trace the development of the process and try to determine why she ended up with this particular picture. Infection of both kidneys is usually the result either of introduction of infection from below or of transmission of infection to the kidneys by way of the blood stream. We know that when an infection persists in the kidney it is usually the result of obstruction to the outflow of

urine from that kidney. I therefore think that we can assume that this woman had some sort of obstructive lesion involving the ureteropelvic junction, the ureter or the terminal portion of the ureter in the bladder, and I see no way of arriving at a definite opinion regarding the location of the obstruction. Obstruction is most frequent at the ureteropelvic junction. On the other hand several things in the history suggest another point of obstruction in this case. Fifteen and again thirteen years before admission to the hospital she had cesarean sections, and following the last section, when an ovary was removed, the wound became infected and drained for four months. We have no record of whether the drainage contained purulent material or urine, but it is possible that this woman had an inflammatory reaction in the pelvis, with periureteritis, which subsequently caused constriction of the lower ureter. Going back still farther in the history we find that as a child she was injured in an automobile accident and presumably suffered a fractured pelvis. There may have been a retroperitoneal hematoma at that time which involved the ureter. Possibly there may have been a congenital stricture of the ureter.

Finally, one other diagnosis that should be considered is tuberculosis, because it is not unusual for a chronic renal tuberculosis to result in stricture of the ureter as an extension of a tuberculous pyelonephritis or for a tuberculous kidney to be infected secondarily with other organisms. There is no way of determining this from a standpoint of reasoning, and I simply point out the fact that there are several possibilities: stricture of the ureter on the basis of injury, on the basis of old infection, possibly on the basis of tuberculosis or on the basis of congenital

abnormality of the ureteropelvic junction. I think that the final episode was the development of a pyonephrosis in which beta-hemolytic streptococci may have been the infecting organisms.

CLINICAL DIAGNOSIS

Carbuncle of kidney

DR. LEADBETTER'S DIAGNOSIS

Pyonephrosis, left

ANATOMICAL DIAGNOSES

Tuberculosis of kidney

Tuberculous peritonitis

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. The preoperative diagnosis was a carbuncle of the kidney. An exploration of the kidney was done, extensive perirenal infection was found and drainage was instituted. At a subsequent operation an attempt was made to remove the kidney, but the disease had already progressed beyond practical operability. It was necessary to remove a considerable portion of the diaphragm and the adrenal gland on that side. The kidney and surrounding tissues showed massive tuberculosis. There was no gross evidence of abscess formation. The patient died some weeks later of tuberculous peritonitis.

DR. LEADBETTER. I should like to point out that chills and fever are extremely rare in renal tuberculosis. In fact it is the exception rather than the rule for a patient with pure renal tuberculosis to have fever of any considerable degree.

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POLITICS AND THE PUBLIC HEALTH

THE administration of a department of health in any large community has become a highly complex problem. It is a professional task requiring considerable training and experience in many and varied fields. The need for such training has given rise to several professional schools in which the curriculum is designed especially for graduates in medicine and for others interested in certain narrower technical fields to prepare them for a career in the control and prevention of disease.

In recent years some legislative bodies have become cognizant of these needs for training and experience in the protection of the public health. They have therefore incorporated into the laws

governing the choice of public-health administrators certain provisions intended to safeguard the public against arbitrary appointments made solely for political expediency rather than for the health and welfare of the people. The requirements in training and experience for these positions are usually made rather exacting, and provisions are also included for consultations with leading authorities within the profession for advice and guidance.

The maintenance and advance of public health is in itself a potent political weapon and in the hands of capable and high-minded chief executives has been encouraged and used to the best advantage. This has meant a careful search for the best talent available, as well as the vigorous support of the chosen servants in the fulfillment of their tasks. It has also been necessary to resist all temptation to yield to pressures to choose politically favored but unqualified or mediocre candidates instead of those best qualified for the task. The recognition of these principles has resulted in the development of outstanding departments of public health in several states and cities, and these in turn have led the country in advancing the health and welfare of its citizens.

Unfortunately, changes in political tides have often brought with them elected representatives of the people who place political interests ahead of the public health and welfare. In so doing, they flout the advice and counsel of leaders in the field of public health and choose their supporters or friends to head the health services of their communities. This has invariably resulted not only in an arrest of progress but also in a deterioration, if not destruction, of the work so tediously and conscientiously built up by their capable predecessors. Not so many years ago Massachusetts went through an experience of this sort, and recently the newly elected mayor of New York City, ignoring and brushing aside the judgment and recommendations of his city's and some of the country's leading authorities, made a purely political appointment, which certainly cannot be construed as following the intent of the law concerning training and experience in public health. It is a great pity that the devoted and conscientious labors that his predecessors in office put into the

maintenance of a high standard in personnel and in performance in New York City's health services should be treated with so little respect and consideration

In New York City, the forces of medical authority and of general opinion in the field of public health sometimes break through political pressures, at least to the point of being articulate in their criticism and in placing the facts before the public. These combined forces resulted in the resignation of the mayor's first appointee, and another attempt was made to obtain a suitable candidate for the position. It was hoped that this time the carefully considered opinion of a committee of recognized experts would not be flouted. But politicians, when they are obviously in error, have an uncanny way of compromising by substituting subservient mediocrity for competent but militant and progressive leadership. Such apparently was the case in the mayor's final choice.* How this will affect the high quality of health services to which the people have become accustomed and what this implies in terms of the health of the people of America's largest city, remain to be seen.

*Deutsch, A. Hacke ran C. H. D. as O'Dwyer rejects top expert. *P. M.* (June 5, 1946)

AVITAMINOSES AND HYPOPROTEINEMIA IN STARVATION

WAR is invariably followed by famine, and advantage of this unfortunate by-product has already been taken by a number of physicians and biochemists interested in nutrition. A few preliminary studies of starvation in occupied countries have appeared,^{1, 2} and it is hoped that the complete reports will soon be published. Severe starvation in prison camps was seen throughout the world and is the subject of a report by Butler, Ruffin, Sniffen and Wickson,³ who examined civilians after their release from Japanese camps. These reports contain a number of interesting and significant observations.

As would be expected, loss of weight was usually severe. For example, Butler et al. reported average losses of 30 pounds for women and 50 pounds for men after three years of internment. In Rotterdam, the average weight loss was 25 pounds.¹

Evidence of gross manifestations of vitamin deficiency was surprisingly uncommon, in fact, with the exception of occasional reports of specific deficiencies, such as those described by Butler et al., they were not observed. Several explanations for this have been suggested. One is that most of the food eaten was unrefined. Thus, in Europe, bread made from coarse flour that contained an assortment of the components of the vitamin B complex, including thiamine, was the staple. On the contrary, polished rice was a principal article of diet of the Japanese prisoners, which may have accounted in part for the evidence of thiamine deficiency that was observed in this group. It is probable that the appearance of a greater number of symptoms and signs of deficiency was prevented by the low caloric value of the food eaten, with an attendant reduction in metabolism, which, in turn, decreased the vitamin requirements.

The incidence of so-called "hunger edema" was high in all the reports. Undoubtedly, in many cases this was due to hypoproteinemia and a consequent reduction in serum osmotic pressure, and in others, especially those studied by Butler et al., to thiamine deficiency. Nevertheless, a significant number of persons with edema were observed in whom the serum protein concentrations were normal and no evidence of thiamine deficiency was apparent. This was true in Holland, where both the albumin and the globulin were determined.¹ In Belgium, Gonnelle⁴ reported 17 cases of edema with serum albumin levels of 4.5 to 5.0 gm per 100 cc. Govaerts and Lequime⁵ studied the serum albumin concentration and osmotic pressure in several cases of this condition and found that the latter was reduced out of all proportion to the former, which was either normal or moderately reduced. Govaerts and Lequime admit that it is difficult to interpret these findings but suggest that reduced tissue osmotic pressure may contribute to edema formation in persons suffering from starvation. Such observations suggest that the Starling hypothesis may not entirely account for "hunger edema." It is apparent that further studies, especially those using new tools, such as the ultracentrifuge and electrophoresis, must be devised to determine the mechanism of edema formation in starvation.

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MASSACHUSETTS MEDICAL SOCIETY

DEATH

ADAMS—Charles S Adams, M D, of Wollaston died June 13 He was in his seventy-eighth year
Dr Adams received his degree from Harvard Medical School in 1894 He was a former president of the Norfolk District Medical Society and a fellow of the American Medical Association
His widow and two daughters survive

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONGENITAL DEFECTS DUE TO RUBELLA

The status of rubella as a completely benign childhood disease was abruptly altered in 1941, when Gregg reported some unusual findings from Australia Following an uncommonly large epidemic of rubella, numerous women were delivered of infants in whom various congenital defects were observed These defects included cataracts and other ocular malformations, deafness, heart defects and defects of the head and extremities Other investigations substantiated these early findings, but the magnitude of the problem has not yet been determined

At present, the Department of Public Health is undertaking a survey to determine whether or not rubella produces similar effects in Massachusetts and, if so, how extensive the problem is The year 1943, which is relatively recent and in which a total of nearly 35,000 cases of rubella were reported, was selected for study Questionnaires are being prepared to go to all physicians in the Commonwealth Descriptive pamphlets and questionnaires will subsequently be sent to each woman, seventeen to forty-nine years of age, reported as having rubella during 1943 The following data are desired the trimester of pregnancy in which the mother became ill, whether there was subsequently a miscarriage, premature delivery or full-term delivery, and whether the infant was normal or demonstrated any congenital defects Negative reports are as essential as positive reports, to establish a comparison

Although 1943 was primarily selected for study, the Department is interested in receiving any information pertaining to this problem, regardless of the date It is essential to establish not only the fact of the condition but also its incidence. Data from all interested physicians, hospitals, schools and other institutions will be welcome

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MAY, 1946

RÉSUMÉ			
DISEASES	MAY 1946	MAY 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	1	1
Chancroid	4	1	*
Chicken pox	2248	1122	1207
Diphtheria	22	14	14
Dog bite	1450	1289	1335
Dysentery bacillary	5	19	12
German measles	1470	167	382
Gonorrhea	340	484	358
Granuloma inguinale	0	2	*
Lymphogranuloma venereum	0	2	*
Malaria	68	146	1
Measles	11501	996	4209
Meningitis meningococcal	8	16	16
Meningitis Pfeiffer bacillus	1	1	2
Meningitis pneumococcal	4	7	7†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	0	3	2†
Meningitis other forms	2	0	1†
Meningitis undetermined	4	2	11†
Mumps	922	2222	1459
Pneumonia lobar	117	261	261
Salmonella infections	3	3	6
Scarlet fever	856	1521	1120
Syphilis	439	388	462
Tuberculosis pulmonary	390	306	303
Tuberculosis other forms	25	18	23
Typhoid fever	2	0	2
Undulant fever	6	2	4
Whooping cough	574	670	671

* Made reportable December 1945

† Four year average

COMMENT

Diseases reported at figures above the seven-year median included diphtheria, German measles, undulant fever, chicken pox and measles The last-named established a new record for this disease for the month, whereas chicken pox reached its second highest peak, the highest having been recorded in 1944

Among diseases reported below the seven-year median were bacillary dysentery, meningococcal meningitis, mumps, scarlet fever and whooping cough

Lobar pneumonia was again reported at a record low for the fourth successive month

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Haverhill, 1, total, 1

Antbrax was reported from Boston, 1, total, 1

Diphtheria was reported from Boston, 2, Brockton, 5, Brookline, 1, Cambridge, 1, Chelsea, 2, Everett, 1, Gloucester, 1, Haverhill, 1, Lynn, 1, Medford, 1, Shirley, 1, Mills, 1, Taunton, 4, total, 22

Dysentery, bacillary, was reported from Grafton (State Hospital), 3, Tewksbury State Infirmary, 1, Milton, 1, total, 5

Hookworm was reported from Lynn, 1, total, 1

Malaria was reported from Abington, 1, Belmont, 1, Boston, 16, Brockton, 2, Brookline, 1, Cambridge, 3, Chelsea, 1, Clinton, 1, Gloucester, 1, Grafton, 1, Haverhill, 1, Hudson, 1, Lawrence, 1, Lowell, 1, Lynn, 1, Malden, 3, Medford, 3, Milton, 1, Newton, 1, Peabody, 1, Plymouth, 1, Quincy, 1, Revere, 2, Seekonk, 1, Somerville, 2, Southbridge, 1, Tann-ton, 1, Templeton, 1, Waltham Regional Hospital, 2, Water-town, 1, West Springfield, 3, Westwood, 2, Winchendon, 1, Winthrop, 1, Woburn, 4, Worcester, 2, total, 68

Meningitis, meningococcal, was reported from Boston, 1, Franklin, 1, Lowell, 2, Malden, 1, Marblehead, 1, Quincy, 1, Weymouth, 1, total, 8

Meningitis, Pfeiffer-bacillus, was reported from North Adams, 1, total, 1

Meningitis, pneumococcal, was reported from Cambridge, 2, Fitchburg, 1, Lynn, 1, total, 4

Meningitis, other forms, was reported from Boston, 1, Winthrop, 1, total, 2

Meningitis, undetermined, was reported from Chicopee, 1, Palmer, 1, Pittsfield, 1, Worcester, 1, total, 4

Salmonella infections were reported from Lawrence, 1, Peabody, 1, Salem, 1, total, 3

Septic sore throat was reported from Boston, 5, Haverhill, 2, Holbrook, 1, Medford, 1, Quincy, 1, Springfield, 1, Westford, 2, total, 13

Tetanus was reported from Chelsea, 1, West Springfield, 1, total, 2

Trichinosis was reported from Medford, 1, New Bedford, 1, total, 2
 Typhoid fever was reported from Springfield, 1, Worcester, 1, total, 2
 Undulant fever was reported from Adams, 1, Ashland, 1, Billerica, 1, Newton, 1, Quincy, 1, Southboro, 1, total, 6

MISCELLANY

Dr Harold J Jeghers, formerly associate professor of medicine at Boston University School of Medicine and a member of the staffs of the Boston City Hospital and Evans Memorial, Massachusetts Memorial Hospitals, has recently been appointed professor of medicine and director of the Georgetown University School of Medicine. He has also become physician-in-chief at the Georgetown University Hospital.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Essentials of Body Mechanics in Health and Disease By Joel E Goldthwait, M.D., LL.D., Lloyd T. Brown, M.D., Loring T. Swaim, M.D., and John G. Kuhns, M.D. With a chapter "The Heart and Circulation as Related to Body Mechanics" by William J. Kerr, M.D. Fourth edition. 12", cloth, 337 pp., with 128 illustrations. Philadelphia: J. B. Lippincott Company, 1945. \$5.00.

The first three editions of this authoritative manual were published under the title *Body Mechanics in Health and Disease*. The fourth edition has been carefully revised and partially rewritten. The chapter on disabilities of the feet has been entirely rewritten, and new chapters on geriatrics and on the heart and circulation have been added. The illustrations have been augmented, and an extensive bibliography is appended to the text. In this edition emphasis is placed on the maintenance of physical fitness and health and on the prevention of many deformities due to faulty body mechanics.

NOTICES

ANNOUNCEMENTS

Dr Edward A. Adams announces that after June 1, 1946, his practice will be limited to general surgery and consultation at 44 Oliver Street, Fitchburg.

Dr William Corwin announces the opening of an office for the practice of psychiatry and neurology at 95 State Street, Springfield.

Dr J. Edward Flynn announces his release from military service and the reopening of his office for the practice of surgery at 475 Commonwealth Avenue, Boston.

Dr Arthur J. Gorney announces his return to the practice of otolaryngology and related plastic surgery at 14 Charlesgate West, Boston.

Dr Patrick J. Mahoney is resuming practice at 96 Bay State Road, Boston.

Dr Jacob Mezer, having returned from military service, announces the opening of his office for the practice of gynecology and obstetrics at 171 Bay State Road, Boston.

Dr John P. Rattigan announces his return from service in the U. S. Naval Medical Corps and the opening of his office for the practice of internal medicine at 422 Beacon Street, Boston.

Dr Benjamin Tenney announces his return from military service to the practice of gynecology and obstetrics at 330 Dartmouth Street, Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The annual meeting of the American Board of Obstetrics and Gynecology was held in Chicago, Illinois, from May 5 to May 11, 1946, at which time one hundred and forty-one candidates were certified.

A number of changes in Board regulations and requirements were put into effect. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, February 7, 1947, at 2:00 p.m. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

Applications are now being received for the 1947 examinations. The closing date for these applications will be November 1, 1946.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, 6.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 11

FRIDAY, JULY 12

*10:00 a.m.-12:00 p.m. Medical Staff Rounds. Peter Bent Brigham Hospital.

12:00 p.m.-1:00 p.m. Clinicopathological Conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

TUESDAY, JULY 16

*12:15-1:15 p.m. Clinicorontgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JULY 17

*10:30-11:30 a.m. Medical Clinic. Isolation Building Amphitheater. Children's Hospital.

*12:00 p.m. Clinicopathological Conference (Children's Hospital). Amphitheater, Peter Bent Brigham Hospital.

*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater. Children's Hospital.

*Open to the medical profession.

MARCH 15-SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.

JULY 9. New England Hospital for Women and Children. Page 878, issue of June 27.

SEPTEMBER 4-7. American Congress of Physical Medicine. Page 616, issue of May 2.

SEPTEMBER 30-OCTOBER 3. Industrial Health Congress. Page 878, issue of June 27.

OCTOBER 6-12. Interamerican Congress of Cardiology. Page xix, issue of June 6.

OCTOBER 7-18. New York Academy of Medicine. Page 544, issue of April 18.

FEBRUARY 7. American Board of Obstetrics and Gynecology. Notice above.

DISTRICT MEDICAL SOCIETY

PLYMOUTH

OCTOBER. Jordan Hospital, Plymouth.

NOVEMBER. Plymouth County Hospital, South Hanson.

JANUARY. Brockton Hospital, Brockton.

FEBRUARY. Moore Hospital, Brockton.

MARCH. Goddard Hospital, Brockton.

APRIL. State Farm Bridgewater.

MAY. Lakeville Sanatorium, Lakeville.

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Number 2

GANGRENE OF THE HAND FOLLOWING TREATMENT FOR PRURITUS OF HEPATOTOXIC ORIGIN*

FRANCIS R. KENNEY, M.D.†

BOSTON

THE treatment of severe pruritus is often so difficult that one is prone to seize on any remedy that seems to offer relief. Many patients enter the hospital with badly excoriated skin, traumatized by their attempts to alleviate the itching, and suffering from lack of rest and sleep. In this report we wish to describe our experiences with a patient suffering from acute hepatitis and jaundice who was given ergotamine tartrate for control of itching and who subsequently developed serious constitutional symptoms and gangrene of one hand.

A 56-year-old, married woman entered the New England Baptist Hospital on January 28, 1945, with a chief complaint of jaundice. This had been present for 2 weeks and was associated with clay-colored stools, dark urine and marked pruritus. For 2 months previously, the patient had been more tired than usual, had lost 10 pounds in weight and had noticed increasing flatulence and belching, with occasional vomiting. Increasing dyspnea with exertion was also present. There had been no severe pain at any time, but there had been occasional mild twinges of discomfort in the right upper quadrant of the abdomen. The past history revealed tonsillectomy 17 years previously, subtotal thyroidectomy for adenomatous goiter 15 years previously and resection of a parathyroid tumor 10 years previously.

System review was negative except for moderate deafness, dyspnea after climbing one flight of stairs, soreness in the right upper quadrant of the abdomen and occasional belching, flatulence and vomiting. The menopause had begun 3½ years previously. The patient had had arthritis for several years.

Physical examination on admission showed a markedly icteric, moderately deaf woman lying restlessly in bed. There were excoriations of the skin of the abdomen and extremities, apparently caused by scratching. All the upper teeth and the lower molars were absent. Tonsillar tabs were present. There was an old thyroidectomy scar. The liver was palpable, both right and left lobes being enlarged, and there was a questionable, rather hard mass between the liver edge and the umbilicus. There were external hemorrhoidal tabs, slight pitting edema of the anterior tibia and marked dorsal kyphosis. Finally, there appeared to be slight arthritic changes of a rheumatoid nature in the fingers. The blood pressure was 140/70, the pulse 72, and the temperature 98.6°F.

The urine had a specific gravity of 1.010 and gave an acid reaction. It contained a slight trace of albumin and no sugar. The urobilinogen was demonstrable in a dilution of 1:8. The sediment contained 7 or 8 white cells per high-power field, a few bacteria and epithelial cells. It contained no bile.

The hemoglobin was 12.4 gm., and the red-cell count 3,580,000. The white-cell count was 6,650 with 68 per cent

neutrophils and 32 per cent lymphocytes. The prothrombin time was 81 per cent of normal. A blood Hinton test was negative. The nonprotein nitrogen was 34 mg. per 100 cc., the total serum protein 8.9 gm., with the albumin 5.3 gm. and the globulin 3.6 gm. The serum bilirubin was 21 mg. direct. The stool was brown.

The clinical impression on admission was carcinoma of the head of the pancreas or stones in the common duct, mild congestive failure and rheumatoid arthritis. On further inquiry, it became known that the patient had received injections of cinchophen for her arthritis during 2 weeks in November, 1944, in another town. In addition, she had received sodium salicylate, iodine, colchicine, streptococcal vaccine and an unidentified stomachic.

As the laboratory work became known and the patient was further observed, the clinical impression changed to that of subacute yellow atrophy based on a toxic hepatitis, in addition to a possible obstruction of the common duct.

The patient was placed on a high-protein, high-carbohydrate, low-fat diet, along with a parenteral preparation of vitamin K and calamine lotion with 1 per cent phenol for the pruritus.

On February 3, a partial gastrointestinal series showed no intrinsic lesion in the upper tract and no widening of the duodenal loop. Daily urine urobilinogen tests were positive in dilutions varying from 1:5 to 1:16. Because of anorexia, infusions of 5 per cent glucose in water fortified with 100 mg. of thiamin chloride were given daily. Two cubic centimeters of crude liver extract was given intramuscularly every 24 hours.

On February 7, because of continued uncontrollable itching, ergotamine tartrate (Gynergen) was started in doses of 1 mg. twice daily. This produced slight to moderate relief.

Amino acids were added to the daily infusions on February 12 and were continued for 6 days. The serum bilirubin rose to 26 mg. 10 days after admission, but since the stools remained brown, the diagnosis of obstruction of the common duct was abandoned. The prognosis appeared poor, even though the serum bilirubin had declined to 12 mg. by February 13. The patient was drowsy, lethargic, anorectic and still jaundiced. The pruritus was fairly well controlled by the ergotamine tartrate.

On February 14, after 16 mg. of ergotamine had been given, it was noted that both radial pulses were weak and that numbness had developed in the right hand. On February 15, the right radial pulse could not be obtained and the numbness persisted, accompanied by aching in the right arm.

On February 17, neither radial pulse was obtainable and there was severe pain in the right hand. On this date a mottled blue-gray color first appeared on the fingers of both hands. This was intermittent and associated with some coldness of the fingers. Pulsations were present in the popliteal, posterior tibial and dorsalis pedis arteries, the feet and toes were warm and there were no color changes in the lower extremities. Although the pain in the right hand persisted, the color changes were inconstant. Ergotamine tartrate was still being given, the total dosage having reached 26 mg. This was immediately discontinued. During the following 24 hours the extremities were unchanged, except that there was a constant dusky, pale-blue color in both hands, which were

*From the Service of Dr. Howard M. Clute and Dr. Thomas J. Anglem at the New England Baptist Hospital.

†Second assistant visiting surgeon, Massachusetts Memorial Hospitals.

cold. In addition, both brachial and axillary pulsations had disappeared.

On February 21 cervical sympathetic block was done, and shortly afterward the patient thought that a little feeling had returned to the fingers of the right hand. Papaverine hydrochloride was given subcutaneously, $\frac{1}{2}$ gr. every 3 hours. Buerger's exercises were started.

Although the right hand was warmer following the sympathetic block, the poor color persisted. Between February 17 and 22, the temperature gradually rose to 102°F. The left hand returned to a normal color within 36 to 48 hours following the cervical block and remained so, with only a sensation of numbness and slight stiffness in the fingers. In addition, the axillary, brachial and radial pulses returned to both arms within 48 hours after the sympathetic block and 72 hours after stopping the ergotamine tartrate.

The patient's general condition improved rapidly. By February 27 the temperature was normal and the anorexia

March 29 and the drug was stopped on April 3, when the patient experienced some anorexia and regurgitation of food, vomiting once. She was out of bed on the 2nd postoperative day and was discharged home on the 9th day, with the wound healing well. Penicillin was discontinued on the day before discharge.

A good cosmetic result was achieved, but it was expected that the function of the hand would be poor, although the stump of the thumb might prove useful. The last report from the patient stated that she was able to write with her right hand.

It seems logical that any pharmacologic depressant of the sympathetic nervous system might give therapeutic assistance in severe pruritus, since it is held by some that an increased irritability of the



FIGURE 1

was markedly diminished. The jaundice became less, and on March 12 the serum bilirubin was down to 2.5 mg. Papaverine was stopped on March 4.

Lines of demarcation began to form on the right hand, and it was evident that gangrene was present. By March 20, the lines between normal and gangrenous tissue were quite plain, and penicillin was started in doses of 100,000 units daily in preparation for operation. Within a few days the lines of demarcation were extremely sharp and the general appearance of all viable tissue was much improved (Fig. 1).

On March 27, the thumb and first finger of the right hand were amputated. During the operation several blood vessels were seen to be filled with old blue-black blood and the vessel walls themselves appeared to be in poor condition. The final pathological report, however, showed no evidence of specific vascular disease and only dry gangrene of the tissues.

Postoperatively the patient did satisfactorily. She was given $1\frac{1}{2}$ gr. of papaverine every 3 hours by mouth, with the thought that any slight dilatation of the vessels would assist healing. This dosage was reduced to $1\frac{1}{2}$ gr. every 6 hours on

sympathetic nerve endings is responsible for this condition. Following this line of reasoning, Lichtman¹ in 1931 reported 4 cases treated with ergotamine tartrate for pruritus, of renal origin in 2 cases and of hepatic origin in 2. All these patients were given 1 mg. three times a day by mouth. In each case an excellent result was obtained shortly after therapy was begun. The drug was stopped immediately on obtaining relief, and no recurrence of the pruritus was noted. Lichtman therefore recommends a dose of 1 mg. orally three times a day as a useful antipruritic in hepatic and renal disease. In addition, the drug is to be stopped as soon as relief is obtained.

In 1933, Snell and Keyes² reported a series of 12 cases in which ergotamine tartrate was used for relief of pruritus. They administered an oral dose of 1 mg three or four times a day or a subcutaneous or intramuscular dose of 0.5 to 1.0 mg daily. They concluded that the pharmacologic action of ergotamine tartrate was so little understood that it would be advisable to regard it as a purely empirical remedy. They reported no toxic effects in their cases, but considered this a possibility. The frequency with which pruritus occurs is brought out in this article, the authors mentioning that this complaint was noted in 60 per cent of patients with choledocholithiasis and in a slightly higher percentage of those with stricture of the common bile duct, especially those of long standing, and in cases in which there was extensive hepatic injury. In neoplastic obstruction itching was encountered in at least 75 per cent of cases.

In 1936, Yater and Cahill³ reported a case treated for severe pruritus by 0.5 mg of ergotamine tartrate three times a day by injection. This was given for six and a third days, the total dosage being 9.5 mg. On the second day coldness of the arms occurred as a premonitory symptom of toxicity, and as a final result it was necessary to amputate both legs halfway between the knee and the foot. No permanent injury to the upper extremities occurred. Microscopic examination showed that all the arteries were constricted to varying degrees and often thrombosed in the less constricted regions. The authors described the two forms of ergotism, the convulsive and gangrenous types.

In the same year, Gould, Price and Ginsburg⁴ described a case in which the patient was thought to be suffering from toxic liver damage, secondary to neoarsphenamine. Because of pruritus, 0.25 mg of ergotamine tartrate was given subcutaneously daily for four days. Following the second injection, pain and coldness developed in the extremities, soon followed by cyanosis and impaired sensation. Both hands also became cold and cyanotic, the dorsalis pedis and tibial arteries could not be felt and the pulsation in the popliteal artery was barely palpable. Ergotamine tartrate was discontinued and the patient was given vasodilators (glyceryl trinitrate and amyl nitrite), as well as strychnine sulfate. Progressive involvement of the legs occurred until there was blackness of the lower two thirds, complicated by skin macerations. There was definite narrowing of the fundal arteries. The patient became worse and died four days after the initial dose of ergotamine tartrate. Post-mortem examination showed all the arterioles examined to be contracted.

In 1939, Comfort and Erickson⁵ presented an excellent review of the untoward effects following the use of ergot and ergotamine tartrate. They also believed that there was no clear, rational explanation for the occasional marked relief noted in cases of pruritus following the use of ergotamine. A brief

review of the literature concerning untoward effects from the use of ergot and ergotamine tartrate was given. They divided this review into groups according to the condition for which ergotamine was given, these groups included puerperal sepsis, menorrhagia, hyperthyroidism, jaundice and pruritus. Following this review, Comfort and Erickson presented 2 cases treated at the Mayo Clinic with ergotamine tartrate in which untoward effects developed. In the first case the drug in oral doses of 1 mg three times a day was given for pruritus, apparently due to stricture of the common duct. A total of 23 mg was given. Following this there developed coldness of all extremities, cyanosis of the right hand and wrist and inability to move the fingers of the right hand. Pulsations could not be felt in the left ulnar or the right radial and ulnar arteries, and could be felt only slightly in the left radial artery. Continuous hot moist packs were applied, and ephedrine was given. In addition to this, alcohol was given by mouth every four hours. On this regime the extremities gradually improved. The final result in this case showed some residual muscular atrophy in the right hand. The second case was diagnosed as metastatic carcinoma of the liver. Pruritus was controlled by one to three tablets of ergotamine tartrate daily. Eight days following admission to the hospital, the radial pulse could be palpated only with the greatest difficulty, and ergotamine tartrate, of which 16 mg had been given, was discontinued. On the next day the pulses were more easily palpable, and the following day they had returned to their normal volume. These authors concluded that some of the untoward effects from the use of one of the preparations of ergot or ergotamine tartrate recorded in the literature have followed the administration of doses larger than those compatible with good practice. In other cases, however, the bad effects have apparently been dependent on the existence of an individual idiosyncrasy to the drug, since extremely small doses have occasionally produced toxic results. In spite of the many reported cases of ergotism, the authors concluded that the value of ergotamine tartrate in doses of proper size, provided adequate precautions are taken, was such that they would continue to use the medication, especially in the control of pruritus and migraine. They emphasized the contraindications to its use and the danger of the development of ergotism, and pointed out that the onset of this complication may be suspected early by frequent examination of the arterial pulsations and of the extremities for spasm and by recognition of its early symptoms. For treatment they recommended pilocarpine subcutaneously, magnesium sulfate parenterally and alcohol orally.

In 1938, von Storch⁶ thoroughly reviewed the literature concerning ill effects following the use of ergotamine tartrate. At that time it was said that the great majority of such effects occurred because

cold. In addition, both brachial and axillary pulsations had disappeared.

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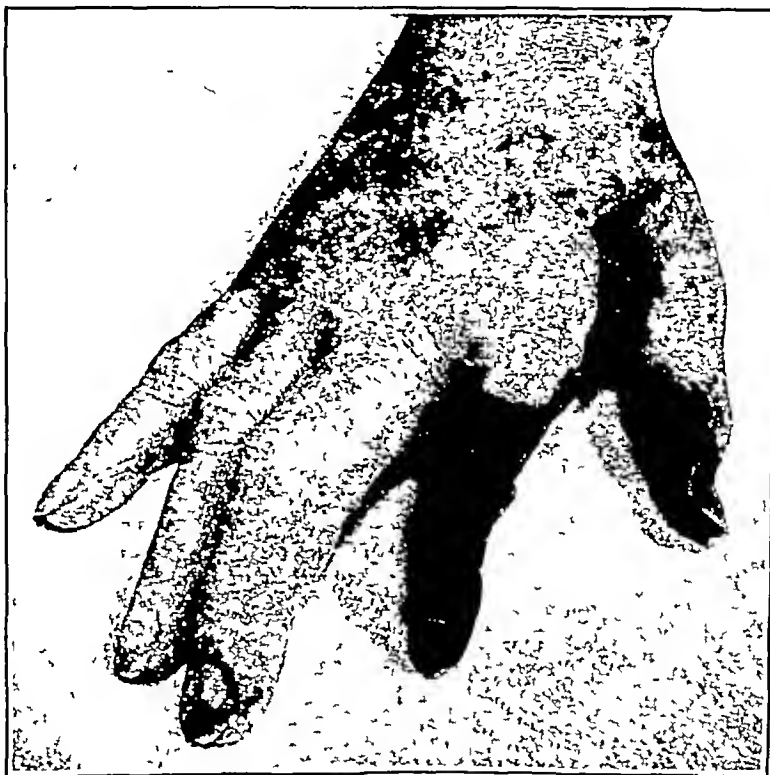


FIGURE 1

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THE DICK TEST IN MILITARY PERSONNEL*

With Special Reference to the Pathogenesis of the Skin Reaction

LOWELL A. RANTZ, M.D.,† PAUL J. BOISVERT, M.D.,‡ AND WESLEY W. SPINK, M.D.§

THE Dick skin test has been widely used for the detection of human beings susceptible to scarlet fever and has proved to be useful for this purpose. It has been demonstrated that a skin rash rarely appears in any but Dick-positive patients during an infection by a scarlatinogenic strain of hemolytic streptococcus. There is no evidence that failure to react to the erythrogenic toxin confers protection against infection by hemolytic streptococci. In fact, recent investigation shows that cases of respiratory infection associated with skin rash caused by these organisms occur much less frequently than do those without a rash, because a large number of highly invasive strains of streptococci are apparently unable to form the skin-reacting substance.

It has usually been believed that the reaction following the injection of culture filtrates of the hemolytic streptococcus in the Dick test is due to the direct toxic action of the products of the organism on the skin.¹ The inhibition of this reaction by the preinjection incubation of the toxin with immune serum, or in vivo in the insusceptible human

being, may then be regarded as an ordinary toxin-antitoxin neutralization. Others have suggested that the phenomenon is the result of hypersensitivity of the allergic type.²

The frequency of occurrence of positive Dick reactions has been repeatedly determined in relation to age³ and geographical distribution.⁴⁻¹⁰ Recently an opportunity arose to investigate the effect of certain geographical and environmental factors on the incidence of positive and negative Dick reactions in a large group of military personnel. The information obtained is presented because a similar group does not appear to have been previously studied in the United States, and because the results permit a reinterpretation of the pathogenesis of the Dick reaction.

METHODS

The skin test was performed exactly as described by the Dicks.¹ All needles and syringes were boiled in distilled water and rinsed with toxin before use. A skin-test dose of toxin (Lederle) contained in 0.1 cc of solution was injected intracutaneously in the flexor surface of the forearm. The test was read twenty to twenty-four hours later and was regarded as positive if the diameter of the area of erythema was greater than 1 cm.

A possible source of error has been introduced by the failure to perform control tests with heated toxin for the purpose of excluding so-called "pseudo-reactions." The Dicks and many others have con-

*This work was done during a field study by the Commission on Hemolytic Streptococcal Infections, Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army Preventive Medicine Service, Office of the Surgeon General, United States Army. The Laboratories of the Department of Medicine, Stanford University School of Medicine, San Francisco, California, were made available to the commission for certain purposes.

†Assistant professor of medicine, Stanford University School of Medicine.

‡Assistant professor of pediatrics, Yale University School of Medicine.

§Associate professor of medicine, University of Minnesota School of Medicine.

of overdosage, pre-existing sepsis or obliterative vascular disease. No serious effects were reported in the author's experience in treating migraine headaches with this drug for the previous five years. He concluded that, although migraine headaches may apparently be treated with considerable success by the use of carefully controlled doses of ergotamine tartrate, its use in the treatment of pruritus is fraught with considerable hazard.

Several experimental studies have been reported in an attempt to clarify the pharmacologic and toxic effects following the administration of ergotamine tartrate. In 1935, McGrath⁷ reported on experimental ergotism produced in the tails of rats treated with ergotamine tartrate. The lesions were quite similar to that of thromboangitis obliterans, with marked cellular proliferation and swelling in the intima, most strikingly seen in the arterioles and small arteries. Administration of theelin protected the rats from pathologic changes, and McGrath concluded that the failure of thromboangitis obliterans to develop in the female was probably due to protection from estrogenic substances.

In 1938, however, Loewe and Lenke⁸ found that theelin and Progynon B were ineffective in preventing the development of gangrene in white rats, even when treatment was begun on the day that ergotamine was first given.

From the previously described cases and others,²⁻²⁵ it becomes apparent that a considerable number of cases of peripheral gangrene have occurred following the use of ergot or ergotamine tartrate preparations. The most important toxic disturbances due to ergotamine tartrate besides gangrene are headache, nausea, vomiting, diarrhea and dizziness. Less frequently observed are weakness, itching, coldness of the skin, thirst, drowsiness, cyanosis, collapse, anginal pain, tachycardia, or bradycardia, muscular twitching or cramps, convulsions, hepatic symptoms and sudden death.

Contraindications to the use of ergotamine tartrate are well summarized by von Storch⁶ as a septic state, cardiovascular disease and obliterative vascular disease. Treatment should be used with caution in cases of arteriosclerosis, hepatic or renal disease and hypersensitivity to the drug. It is certainly most strongly to be recommended that careful daily palpations of the radial and ulnar arteries, along with those of the posterior tibial, popliteal and dorsalis pedis arteries, be carried out in all cases in which ergotamine tartrate is being used for the control of pruritus. The patient should also be carefully questioned for any symptoms of numbness, tingling, coldness or pain in the extremities. Should any of these symptoms or signs be noted, the drug should immediately be stopped and measures taken to promote peripheral circulation. These measures include the intravenous use of papaverine hydrochloride and the oral use of ephedrine, papaverine hydrochloride and alcohol. Magnesium sulfate

intravenously or 1 per cent pilocarpine subcutaneously may be helpful. Roch²³ has suggested acetylcholine. In this condition, however, by far the most effective treatment is prophylaxis which consists of the immediate cessation of ergotamine tartrate therapy when any of the previously mentioned signs are noted. It cannot be too strongly stressed that most careful daily observation of the patient by the physician in charge is essential for the safe administration of this medicine. The physician who is driven to its use for the control of intractable pruritus should be well aware of its dangers and be prepared to take immediate steps to counteract them.

CONCLUSIONS

In treating severe pruritus one should be careful in the choice of a therapeutic agent, with regard to the possible toxic effects. The worse is the general systemic condition of the patient, the greater is the danger of toxicity from drugs used to control pruritus.

Ergotamine tartrate is definitely useful as an antipruritic agent provided one realizes the potentialities for severe reaction in its use.

If ergotamine tartrate is to be used as an antipruritic, the following precautions seem indicated. The dose should not exceed 1 mg three times a day orally. At least once daily, and preferably twice, the patient should be questioned and examined concerning pain, coldness, cyanosis, loss of arterial pulsations, impaired sensation and tingling in the extremities. Should any of these signs or symptoms develop, the drug should immediately be discontinued and appropriate therapy started.

Therapy for ergot poisoning following the use of ergotamine tartrate includes the following: papaverine hydrochloride (0.02-0.03 gm) intravenously or orally or both, ephedrine (24 mg) orally, alcohol (15 cc every four hours) orally, magnesium sulfate (15-20 cc of a 3 per cent solution intravenously), 1 per cent pilocarpine (1 cc subcutaneously), acetylcholine, and sympathetic block with novocain.

The use of ergotamine tartrate is contraindicated in the presence of a septic state, cardiovascular disease and obliterative vascular disease. It should be employed with great caution in cases of hepatic or renal disease, arteriosclerosis and hypersensitivity to the drug.

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positive Dick reactions in relation to this factor was determined. The data, classified by geographical regions, are presented in Table 4. The incidence of

incidence of hemolytic streptococcus respiratory disease, was not followed by an increase in the frequency of negative Dick reactions.

TABLE 4 Relation of Preliminary Residence to Dick Positivity

AREA*	No of Men Studied	Dick Positive	
		No	PERCENTAGE
1	127	50	39.3
2	152	59	38.8
3	121	32	26.5
4	80	16	20.0
5	100	14	14.0
6	114	11	9.6
7	103	9	8.7
8	267	84	31.4
9	90	30	33.3
10	34	10	29.4
11	92	38	41.3

*The areas are as follows: 1—New England: Maine, New Hampshire, Vermont, Massachusetts, Connecticut and Rhode Island. 2—New York. 3—North Atlantic states: Pennsylvania, New Jersey, Delaware and Maryland. 4—Middle Atlantic states: Virginia, North Carolina and South Carolina. 5—border states: West Virginia, Kentucky, Tennessee. 6—South East: Georgia, Florida, Alabama, Mississippi, Louisiana and Arkansas. 7—South West: Texas, Oklahoma, Arizona and New Mexico. 8—Great Lakes states: Ohio, Indiana, Illinois, Michigan, Wisconsin and Minnesota. 9—Middle West: North Dakota, South Dakota, Nebraska, Kansas, Iowa and Missouri. 10—Rocky Mountain states: Montana, Idaho, Wyoming, Colorado and Utah. 11—Far West: California, Washington and Oregon.

positive Dick reactions was extremely high (38.8 to 41.3 per cent) among those who had lived in New England, New York or the Far West, it was lower (20.0 to 33.3 per cent) among those from the remainder of the North, Middle West and West, and extremely low (8.7 to 14.0 per cent) in the border states, the Southeast and the Southwest. These differences are very great and of unquestionable statistical significance. As an added check, the duration of military service and age of men in the low-incidence areas were studied and discovered to approximate the distribution of these factors in the group as a whole.

DISCUSSION

Certain information obtained during this study is of general interest. Slightly more than 25 per cent of white American men of military age were Dick positive. The frequency was increased below and decreased above the age of twenty, but the differences were not great. These facts are in accord with previous investigations in the United States.

The incidence of positive Dick reactions was the same in men admitted to the hospital with virus-type respiratory disease as in those with Group A hemolytic streptococcus sore throat, demonstrating that there is no relation between the Dick reaction and immunity to infection by hemolytic streptococci. This fact has been previously established¹¹ but has been insufficiently emphasized.

It is also worth while to record the information that men become less frequently Dick positive with prolonged military service. This effect did not become manifest before the end of the twelfth month. As much as one year of service in the study post, which was located in an area of extremely high in-

Although this theory of the pathogenesis of the Dick reaction has been widely accepted, it is not in accord with most of the studies that have been made for the purpose of elucidating it. Most important is the established fact that infants are Dick negative regardless of the reaction of the mother or the presence or absence of antitoxin in her or in the infant's serum.¹²⁻¹⁴ Most of these babies later become Dick positive, but do so at irregular intervals. Children of various ages who have been tested over considerable intervals of time have been observed frequently to acquire but rarely to lose the ability to react to the erythrogenic toxin.^{15, 16} Maternal antitoxin transferred through the placenta should disappear promptly in children, and all subjects capable of becoming Dick positive should have done so by the end of the first year of life. More elaborate experiments have demonstrated that it is possible to transfer passively Dick positivity to Dick-negative subjects by the transfusion of serum.¹⁷ In addition, it has been pointed out that the streptococcal erythrogenic toxin is much more heat stable than the other well known bacterial toxins.

All these facts, and others not described, have been correlated in an interpretation that states that the ability to react to Dick toxin is not a natural characteristic of human beings but is acquired as the result of exposure to the hemolytic streptococcus, and that it is a hypersensitivity phenomenon of the allergic type.²

A comparison of the geographical incidence of positive Dick reactions and of hemolytic streptococcus sore throat might permit a decision which of the two mechanisms described above is correct. If the ability to react to Dick toxin is a natural characteristic that may be lost by exposure to hemolytic streptococci and the subsequent development of immunity following clinical and inapparent infection, the incidence of positive reactors should be low in areas where streptococcal disease occurs frequently and high in those in which this disease is

sidered this precaution to be unnecessary with suitably prepared testing materials. The observed positive reactions appeared to be of the correct type and were reversed during convalescence from scarlet fever in the expected manner.

RESULTS

The reaction to Dick toxin of 1280 white men suffering from acute respiratory disease admitted to a large station hospital was determined on the second hospital day. There was no discrimination, all cases during the study period being included. The test was positive in 27.8 per cent. Three hundred and ninety-seven of these men were believed, on clinical and bacteriologic grounds, to suffer from Group A hemolytic streptococcus sore throat. Twenty-four developed a typical scarlatinaform rash. A significant antistreptolysin or antifibrinolysin response or both was observed in 87.9 per cent of 342 of these patients in whom suitable tests were done, indicating that the clinical impression was usually correct. The Dick test was positive in 27.7 per cent of this group. The relation of the results of this test to the clinical course of hemolytic streptococcus respiratory disease will be presented elsewhere.

The disease was clinically compatible with a virus type of infection in 803 cases, and no Group A hemolytic streptococci were isolated from the nasopharynx. Of these men, 27.2 per cent were Dick positive. In another 80 patients the diagnosis was not clearly established on clinical and bacteriologic grounds. These infections appeared to be examples of virus-type respiratory disease occurring in persons who were nasopharyngeal carriers of Group A hemolytic streptococci. An antibody response was demonstrated in only 2 of 18 cases studied in this group. Thirty-five per cent of these patients were Dick positive.

Age

The relation of age to positive Dick reactions is presented in Table 1. Men over the age of twenty

TABLE 1 *Relation of Age to Dick Positivity*

AGE	NO. OF MEN STUDIED	DICK POSITIVE	
		NO.	PERCENTAGE
5 yr.			
17 to 20	407	143	35.1
21 to 24	397	92	23.1
25 to 30	290	64	22.1
31 to 35	128	35	27.3
36 and over	49	15	30.6

react to Dick toxin in less numbers than do younger men. The groups are large and the results are of statistical significance. A precise analysis was not made, but it is logical to assume that men in the older age groups frequently had had a more pro-

longed military service, which, as will be demonstrated, decreases the incidence of positive Dick reactions.

Duration of Military Service

When the study group was considered in relation to the duration of military service, it was discovered that the incidence of Dick positivity was high (34.3 per cent) in men who had been in the Army for less than a year and fell abruptly to much lower levels (22.0 per cent) among all those who had served for a longer period of time. No significant difference existed in the rate of six-month periods of service from thirteen to more than thirty-six months. The essential data are presented in Table 2.

Duration of Service in Study Post

This survey was conducted in an Army camp located in an area in which hemolytic streptococcus

TABLE 2 *Relation of Military Service to Dick Positivity*

DURATION OF SERVICE	NO. OF MEN STUDIED	DICK POSITIVE	
		NO.	PERCENTAGE
mo			
0 to 6	181	62	34.3
7 to 12	429	147	34.3
13 to 18	306	73	20.3
19 to 24	118	30	28.1
25 to 36	121	22	18.9
36 and over	125	22	18.0

disease was exceedingly frequent. Approximately one third of all cases of respiratory infection admitted to the station hospital were caused by this organism. It was of interest to ascertain whether prolonged service in this post could be demonstrated to modify the incidence of Dick positivity. The

TABLE 3 *Relation of Duration of Service at Study Post to Dick Positivity*

DURATION OF SERVICE AT STUDY POST	NO. OF MEN STUDIED	DICK POSITIVE	
		NO.	PERCENTAGE
mo			
Less than 1	705	202	28.6
1 to 6	277	67	24.2
7 to 12	232	69	29.7
13 and over	61	18	29.5

essential data are presented in Table 3. No significant alteration in the frequency of positive Dick reaction occurred after men had served in the study post for twelve months. Consideration of the effect of more than one year of residence was impossible because insufficient personnel had been stationed there for a longer period of time.

Premilitary Residence

The premilitary residence of all the tested men by states was ascertained, and the frequency of

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PRIMITIVE MEDICINE*

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PHILADELPHIA

ANY discussion of so-called "primitive medicine" must begin with an essential clarification. When one speaks of primitive medicine, one refers to a special body of traditional knowledge which compared with that of the present appears crude and undeveloped. It is desirable to remember that this lack of development is a function not of the group's biologic status but of its cultural status, and that its cultural status is, again, a function not of its biologic makeup but primarily of the history of its experience as a social group.

The comparatively undeveloped medical knowledge and practice of isolated man is simply a reflection of the fact that such a person has not experienced the kind of culturalizing conditions that have fallen to the lot of man living in the Western world. The former has not developed so complex a culture as has Western man, for the reason that he has been completely isolated from the main stream and cross currents of cultural interchange and development to which man in the Western world has been exposed. Any reference to the medicine or culture of isolated man — a phrase in many ways to be preferred to the usual "primitive man" — in terms of inferiority to our superior selves is to be deprecated. To compare the cultural achievements of any two groups for the purpose of valuation, it is first necessary to determine whether they have had the same or similar opportunities for cultural achievement.

Compared with the history of experience and opportunity that Western man has enjoyed, that of isolated man has been of the most minimal kind. This fact should sufficiently account for the cultural differences that one observes, as a whole, to exist between them, and it should explain the

comparative lack of complexity that characterizes the medical knowledge of isolated man.

However ridiculous and stupid some of the medical beliefs and practices may appear to the sophisticated Westerner, it should be enough here to say that this attitude is but a confession of ignorance and a lack of a historical sense and something of human understanding, for the medical lore of isolated man represents a perfectly harmonious part of the acquired wisdom of the group and a thoroughly integrated part of the social structure as a whole. Occurring in the culture in which it does, it could hardly be other than it is.

The time has long since passed when the medical lore, the leechcraft, of isolated peoples could be classed with the quaint and queer in the album of medical curiosities. Nor is it sufficient to record the bare details of that lore, as is almost invariably done in present-day histories of medicine. Medicine is a social phenomenon, and the medicine of any people can only be effectively understood as such. For this reason it is necessary to gain an understanding of the society as a whole if its medical knowledge and practice are to be understood in their full significance — if, indeed, that knowledge and practice are to be understood at all. This is particularly the case in isolated societies, in which medicine is much more closely integrated with the institutions and beliefs of the society as a whole than it is in the highly diversified structures of Western societies. Failure to recognize these elementary facts makes the chapters on primitive medicine in contemporary histories of medicine their least satisfactory ones.

Special studies of the medicine of several primitive peoples that have been written by physicians with anthropologic training are now available, and there is a vast amount of material to be found in the field studies of anthropologists.¹⁻¹⁴ There is a serious need of additional special field studies of the medicine of particular primitive peoples, but until these have been carried out, a highly desirable step

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rare. On the other hand, if a positive Dick reaction is the result of hypersensitivity acquired by exposure to the hemolytic streptococcus, the exact reverse should occur.

When the data on the geographical distribution of Dick positivity obtained during this study are considered, it is discovered that the latter situation prevails. It is difficult to state accurately the frequency of hemolytic streptococcus respiratory infection throughout the United States, but extensive studies of acute respiratory disease in military personnel and inspection of the distribution of cases of scarlet fever and rheumatic fever in the armed forces and in the civilian population indicate that the hemolytic streptococcus is rarely the cause of respiratory disease in the southern states¹⁸⁻²². Elsewhere this organism is known to be responsible for a large but unknown percentage of infections of the respiratory tract. It seems quite certain, therefore, that men whose premilitary residence has been in an area in which streptococcal disease occurs infrequently are rarely Dick positive.

An examination of published studies reveals that this fact has been previously established. A careful study in Rio de Janeiro^{6, 6} showed that scarlet fever was extremely infrequent and that Dick-positive persons were rare in all age groups. Many other investigations⁴⁻¹⁰ have confirmed the fact that positive Dick reactions are infrequent in the Tropics and in isolated Arctic communities where streptococcal disease is usually believed to be infrequent²³. The fact that these surveys were carried out in a variety of racial groups in areas in which the incidence of streptococcal disease had been poorly assessed detracts from their usefulness.

The frequency of positive Dick reactions in a large number of Chinese students from all sections of the country was determined by Lai.⁷ Those who had lived in northern China, where scarlet fever is widespread and severe, showed a frequency of positive reactions three times that of those whose residence had been in the tropical provinces, where the disease is rare.

It may be said to be established that the incidence of positive Dick reactions is low in the parts of the world in which infection by hemolytic streptococci is an infrequent occurrence. The possibility that this is due to racial variations is eliminated by the study of homogeneous population groups in China and in the United States.

Previous workers have believed that this phenomenon is to be explained on the basis of a high natural immunity to the streptococcus toxin, although at least one observer failed to find circulating antitoxin in the serum of Dick-negative persons in the Tropics.⁸

The present study strongly suggests that a hypothesis based on natural immunity is in error, since there appears to be no reason to suppose that white residents of the southern United States should have

natural antibodies differing from those present in persons living in the North.

Since Dick positivity and hemolytic streptococcus infection occur infrequently in certain areas, and the reverse is true, the inescapable conclusion is that contact with the streptococcus is essential for the establishment of skin reactivity to the erythrogenic toxin. If this is the case, it is impossible to regard this material as a true toxin, and the skin reaction must be regarded as a hypersensitivity phenomenon. It is recognized that this skin reaction is somewhat different from others of an allergic nature, since it may be readily reversed during convalescence from scarlet fever or by active immunization. That this may be due to desensitization rather than to true toxin-antitoxin neutralization has been suggested.²

If the conclusion is acceptable that exposure to streptococcal infection is necessary for the establishment of a positive Dick reaction, the frequency of positive reactors in a population may be used as a rough guide to the incidence of streptococcal infection in the group. The occurrence of nonscarlatigenic strains of Group A streptococci suggests an important source of error in such a procedure, since many examples of streptococcal disease occur in certain populations as the result of infection by such streptococci but sensitization of the affected persons may not result.

SUMMARY

The reaction to Dick toxin of 1280 white men of military age was studied.

The frequency of positive reactions was least in men over the age of twenty and in those who had had more than twelve months of military service.

Positive Dick reactions were infrequent in men whose premilitary residence had been in a geographical area in which the incidence of hemolytic streptococcus disease is known to be low.

It is concluded that exposure to the hemolytic streptococcus is essential for the establishment of a positive Dick reaction.

The Dick reaction is probably the result of acquired hypersensitivity to the products of the streptococcus rather than of a natural susceptibility to a true toxin.

We are indebted to Miss Elizabeth Randall, who performed all the skin tests, and to Mrs. Helen Rantz, who compiled the data.

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drugs as quinine, curare, opium and digitalis, to name but a few, were all discovered by isolated peoples as specifics for certain conditions, and that in such practical phases of medicine as surgery many serious operations have, from earliest times, been performed on human beings with complete success. Fractures of every sort have been repaired, dislocations corrected, and obstructions removed.

This paper will attempt a brief inquiry into the types of disease concepts that are to be found in the cultures of isolated peoples, and their classification, so that they may be efficiently compared and articulated with those of the technologically more advanced Western world.

As a basis for comparing the medical concepts and practices of isolated peoples with those prevailing among the peoples of Western societies, three causes may be recognized that are universally known to explain disease. The first is natural cause, the second is human agency, and the third is supernatural agency. If the disease can be explained in terms of material agencies, it is attributed to natural causes, but if it is attributable to the action of some human being who has, for example, resorted to sorcery, the malady is assigned to a human agency. Finally, if the illness is held to be due to some spiritual or supernatural being or principle it is ascribed to the direct action of the supernatural.

The three possible causes of disease here stated are those that, among sophisticated and isolated peoples alike, are accepted the world over. The principal difference between the concepts held by peoples with widely differing cultures is that groups with greater educational advantages—in the Western sense of those words—tend to place more confidence in the natural causation of disease, whereas isolated peoples tend to place more confidence in its supernatural causes. As everyone is aware, even in our own society there are really very few persons who do not retain some belief in the supernatural causation of disease, nor is it necessary to point out that the less educated a person is, the likelier he is to place his faith in the supernatural explanation of disease. In many parts of Europe there exist at the present time populations who believe quite as much in the supernatural causation of disease as do the most isolated peoples.*

When a man can come more or less closely to discerning the empirical elements in a situation, his reasoning is likely to be logical and based on common sense. On the other hand, when the situation with which he is concerned defies such definition, he tends to accept explanations that are no more explicitly denotable than are the conditions with which he is dealing ‡

*For an admirable study of the folk medicine of a European peasantry—of the Balkans in this instance—see Kempf¹⁶ and Brendle and Unger¹⁷.

†Any object to which the human organism can react serially point for point may be referred to as 'explicitly denotable'. The objects known as 'finger' or 'penny' or 'stone' belong to this class. Such entities as 'Fascism', 'democracy' and 'nation' to which a person cannot react in this way are denoted by terms referable to 'implicit language usage'.¹⁷

In most isolated societies it is a firm tenet of belief that the world is animated by some spiritual principle or power. This, in fact, is the definition of the supernatural—namely, the belief in the unseen, mysterious and wonderful spiritual force or powers that pervade the universe. The supernatural is generally personified in the form of a being or several beings, each with particular powers that greatly transcend anything of which man alone is capable. This belief is called "animism" by anthropologists. The power of the supernatural may also manifest itself in a disembodied form, as a supernatural quality or an attribute of objects, just as color, weight and hardness are attributes of objects. Examples are the "orenda" of the Iroquois, the Algonquian "manitou" and the Melanesian "mana". This form of the belief in the power of the supernatural is known as animatism ‡.

In passing it may be noted that primitive religion may be regarded as the technic and result of supernaturalism. Religion differs from magic in that it makes no attempt to coerce but is directed toward entering into closer personal relations with the supernatural, one prays, beseeches or worships, but one never controls §.

In animistic societies it is, of course, a simple matter to explain almost everything of unknown causation as due to the activity of good or evil spirits. Magic consists of compelling these spirits to do one's bidding. Their manipulation for evil purposes is sometimes called "black magic," whereas their manipulation for good purposes is called "white magic." The practice of magic in any form is called "sorcery."

At the very outset one sees how intimately related to the character of a culture are the concepts of disease that it holds, for it is obvious that in a sophisticated society in which the experimental method occupies a prominent place, the doctrine of natural causes will be the one most generally accepted as an explanation of disease. Where the habit of thought associated with the experimental method is wanting and spiritistic beliefs are the dominant ones, the tendency will be to explain disease in terms of the supernatural.

CLASSIFICATION OF DISEASE CONCEPTS

Given the cultural character of a typical isolated society, there may be recognized seven main types of primitive disease concepts. These are as follows: sorcery or magic, breach of taboo, disease-object intrusion, spirit intrusion, soul or body loss, dreaming and independent occurrence.

‡There is serious question whether the distinction between animism and animatism can be legitimately maintained since in the final analysis the supernatural attributes of an object may be traced back to some definitely recognized personified spiritual agency. For an excellent discussion of this matter see Karsten¹⁸.

§In the discussion of these matters it is well to remember that there are no attitudes toward supernatural relations that are not taken toward human relations. Honor and awe are not given to human beings to the extent to which they are shown toward the supernatural beings: the gods. The only difference is one of extent.

would be a stocktaking of what is already known and an attempt at an analysis and systematization of this at present widely scattered knowledge. The attempt would be an extremely rewarding undertaking, and it is one that merits the attention of the serious student.

At this point I should like to discuss briefly the time-honored and perennial error that seems to have established itself in the minds of many writers on the subject — namely, the idea that both medicine and science grew out of magic. Magic may be defined as the process of manipulating the supernatural, of coercing or procuring it to do one's bidding by the performance of certain ritual acts. Science may be defined as verifiable and communicable knowledge, based on observation, experiment and reflection — in short, on doing one's utmost with one's mind, as Percy Bridgman has so fittingly put it. Now, magic and science both deal with causation, — magic with supernatural causation and science with natural causation, — and the reliance that people put on these two ways of manipulating the world in which they live is well-nigh universal. Both magic and science are mechanical procedures, but whereas the purpose of the former is the compulsion of the supernatural according to letter-perfect traditional rules of thumb, the latter has no place whatever for the supernatural, which is the main concern of magic. Science deals with cause-and-effect sequences in the natural world — experimentally gauged and determined. Magical cause and effect represent nothing but fabrications of the human mind operating in an imaginary world — the supernatural. Magic is based on a series of false analogies, whereas science is based on a rigorous testing and verification of repeatable experiences.

Every people defines the natural and the supernatural in its own way, but there is general agreement on the essential principles involved. It is only in certain sophisticated areas of Western society that some men have definitely discarded the picture of the universe as operating on two parallel and contrasted sets of causation. Primitive peoples recognize ordinary natural sequences of cause and effect, just as they also recognize more wonderful causations, — the supernatural, — technics that are not checked against natural laws but are solely concerned with manipulating a special potency that has its own rules apart from the matter-of-fact ones of craft and industry.

To manipulate the natural world man everywhere develops a material technology. No living or extinct people of whom there is any knowledge is ignorant of technologic facts. The very process of getting a living, even at the simplest imaginable levels, demands the development of certain technologic processes for manipulating the environment. The material culture of isolated peoples everywhere abundantly testifies to their ingenuity, inventiveness and technologic proficiency.

It should be fairly clear that where material technology is present, — and it is present in all human societies, — it becomes quite unnecessary to derive science from anything other than the development and practice of the technics involved and the reflecting and philosophizing on them in which man everywhere is wont to indulge.* A simple diagram will illustrate the actual relations. To manipulate the natural world man develops a material technology, and it is out of this that science eventually grows. To manipulate the supernatural

Natural World Technology	Supernatural Magic
Science	

world he develops a series of magical technics. There is no necessary association between the one and the other.

Close study of the conditions actually prevailing in isolated societies reveals the fact that magical and scientific activities are frequently pursued as parallel activities quite independently of each other. For example, to restrict the discussion to the medical referent, when a limb is broken it is set in accordance with the best available empirical knowledge that the native doctor as a highly specialized member of the tribe has been able to obtain. No magic or ritual is involved in the treatment of the injured limb. When a person has suffered from severe and prolonged headache his skull may be trephined, and if he does not get better it is trephined until he does — or dies. No magic is involved in this either. In short, isolated peoples have their rational medicine, which is based entirely on experience and into which no element of the magical enters. Experience has taught them that certain plants possess specific qualities of medicinal value, they are therefore rationally used, and so it is with many other facts and practices that have been acquired and developed through experience. Isolated peoples also have their magical medicine, in which the principal reliance is placed on the compulsion of the supernatural. All this is not to say that magical medicine and rational medicine or science are always unrelated, for the fact is that they are frequently related, and it is often quite difficult to disentangle them. This is, however, to say that persons who are members of isolated societies are by no means fools, and that they do not live under the unrelieved domination of a host of magical ideas and practices. Nor are they, as some writers have suggested, characterized by a prelogical type of thought. If anything they suffer from an excess of logic rather than from a deficiency of it. It is an interesting fact that such

*For primitive man as a philosopher see Paul Radin in *On the strictly scientific accomplishments of isolated peoples*. Professor Wilson Wallis of the University of Minnesota has gathered together a vast amount of material. This work is about to be published.

internal organs, the thin walls of which when they do not receive an adequate supply of oxygen become more and more permeable to the fluid part of the blood. Plasma escapes into the perivascular spaces, with a resulting high concentration of red corpuscles, and the victim dies of shock scarcely distinguishable from true wound shock.

To return to taboo, Webster ²⁰ writes

The authority of a taboo is unmatched by that of any other prohibition. There is no reflection on it, no reasoning about it, no discussion of it. A taboo amounts simply to an imperative thou-shalt-not in the presence of the danger apprehended. That any breach of the prohibition was unintentional or well intentioned matters nothing, no allowance is made for either the ignorance or the praiseworthy purpose of the taboo-breaker.

When sickness is believed to be produced by the breach of some taboo, expiation of the offence may sometimes be made with the assistance of a medicine man, who, by the performance of certain magical acts, may succeed in releasing the victim from the effects of his transgression.

Disease-Object Intrusion

In isolated societies it is a widespread belief that many types of illness are caused by the entrance into the body of some foreign object. Such morbid objects may find their way into the body either by direct human agency or by the action of some nonhuman agent. The disease object is usually regarded as carrying a spiritual essence, which is the real cause of the illness. Under such conditions it becomes the function of the medicine man to extract this object from the victim's body. The disease object may take almost any form, but it is always extremely small—a pebble, a splinter of wood or bone, a hair, an insect, a lizard or a worm. Removal of the object is usually accompanied by sucking on some part of the body, and in a short time the medicine man produces the pathogenic object from his mouth. This has, of course, been secreted there by him for production at the appropriate time, in much the same manner as many a modern physician, called on to deal with a patient who mistakenly believes that a fishbone has lodged in his throat, produces a fishbone that was never there. In either case the patient leaves perfectly happy in the knowledge that he will be troubled no longer. Since in many cases the illness was originally produced by suggestion, the sight of the object believed to have been the immediate cause of the disease is sufficient to work a cure.

Spirit Intrusion

When it is believed that disease is due to the presence in the body of some immaterial agent, such as a spirit, a ghost or a demon, one may speak of disease by spirit intrusion. This must be carefully distinguished from spirit possession, the latter resting on the belief that a person has been entered by a supernatural being, who then speaks through his host.

Such a person is not regarded as ill in the ordinary sense of the word. His insanity is, on the contrary, regarded as evidence that he has been honored by a supernatural being who has taken abode within the affected person's body. He is therefore respected as a holy one and is often consulted as an oracle.

There are three methods ordinarily used to eject the intrusive spirit from the victim's body—exorcism, mechanical extraction and transference. In exorcism, the evil spirit is ejected by conjuration. The spirit is removed by manipulative, surgical or similar means in mechanical extraction. Transference refers to the transfer of the disease object from the victim's body to some object. Exorcism is nearly always practiced together with one or both of the other methods.

Soul or Body Loss

Abstraction of the soul or a part of it or some part of the body is still another mode in which disease is believed to be produced. Among the Australian aborigines the abstraction of the kidney fat, or perhaps more correctly the fat of the greater omentum, is held to be a common cause of disease. It may be removed by sorcery as a punishment for the infringement, knowingly or unknowingly committed, of some rule, thus bringing about the death of the victim ²¹. Still more widespread is the belief in soul abstraction as the cause of disease and often of death. The soul may be abstracted by ghosts or sorcerers, or during sleep the soul may leave the body—as it is frequently believed to do in dreams—and meet with some accident on its nocturnal wanderings that prevents its return. The task of the medicine man is to discover the whereabouts of the missing soul by divination or other means and return it into the body of his patient.

Dreaming

Dreams may be the cause of sickness. In the Pacific and in the southwestern areas of North America, one may dream that one has eaten poisoned foods or that an animal has entered one's body, and wake up or fall ill shortly afterward. Furthermore, the dreamer may not himself suffer from the dream, but a relative of his may be afflicted.

Independent Occurrence

Minor ailments, such as leg sores, cuts, scratches and a host of other minor conditions, are regarded as arising independently of any action on the part of human beings or of higher powers. It is when a disease appears to threaten life that people begin to think of human or spiritual agencies. Attracting little attention, minor ailments do not afford material for speculation. When Rivers²² inquired of the Eddystone islanders of Melanesia what caused these minor ailments, they replied that they came of themselves and were not, therefore, the occasion

Sorcery or Magic

When it is believed that disease is produced by the activities of persons skilled in magic or by the manipulations of older persons who exercise some control over the supernatural, the disease is said to be produced by sorcery or magic. In isolated societies there are generally available a number of magical ritual formulas that can be enacted by anyone to compel the supernatural to produce disease and even death in some other person, whether of one's own or another tribe. In addition there is always present a special class of persons, the medicine men, who are particularly skillful in manipulating the supernatural for good or evil. These may be hired at almost any time to bring affliction to one's enemies.

The magic by which these conditions are produced is of two kinds, homeopathic or imitative magic and contagious magic. Homeopathic magic assumes that things that resemble each other are the same. An image, for example, is made of one's enemy and this is injured or destroyed, in the belief that the victim will thereby be injured or destroyed.

Contagious magic makes the assumption that things that have once been in contact are always in contact, therefore, whatever is done to the one must similarly affect the other. According to this view, a person is never really dissociated from any part of his body or anything that has been in contact with it. Thus, his nail parings, hair, spittle and clothing are all part of him, so that anyone who obtains possession of these can, at any distance, work his will on the person of whom they were once a part.

In practice both homeopathic and contagious magic are often combined, more exactly, whereas homeopathic magic may be practiced by itself, contagious magic will generally be found to involve an application of the homeopathic principle. Both branches of magic are comprehended under the general name of "sympathetic magic," since both assume that things act on each other at a distance through a connecting invisible ether.

Under such conditions of belief, causation of disease by sorcery is brought in to explain not only illnesses that have no obvious antecedent cause but also those in which the natural cause is obvious. For example, when a man stumbles and bruises himself or falls from a tree and injures himself, the cause is not ascribed to the boulder that was in the way or the rotten branch that broke or to some failure of co-ordination on the part of the victim. Instead, the accident, as one may loosely call it, is attributed to the act of a sorcerer.

Among the Australian aborigines, for instance, as among many other isolated peoples, death is never regarded as due to natural causes but is always ascribed to sorcery. With the assistance of a medicine man, the person responsible for causing

the death is then usually discovered and subsequently becomes marked for death.

Since the magical practices of the sorcerer are, to a large extent, part and parcel of the religious system of groups, it will be readily understood that religion and primitive medicine are closely associated with one another — an association that in civilized societies has been attenuated but never quite dissolved. With few exceptions, the diagnosis, treatment and prognosis of disease are all made by the medicine man, and when he is able to discover the cause, as he usually is, he can generally neutralize the effects of the maleficent spirits by some countermagic. When the disease object is capable of being abstracted directly from the victim's body, such abstraction is a simple matter for an expert medicine man. It is only in certain cases of breach of taboo that he, or anyone else, can do nothing.

Breach of Taboo

Taboo (originally a Polynesian word) may be defined as a prohibition the infringement of which automatically brings about its own punishment. Certain things are regarded as in themselves so dangerous that to break the taboo in connection with them results automatically in punishment without the mediation of supernatural or human forces. The occult power residing in a mystically dangerous object is transmissible and is therefore capable of affecting whatever comes into contact with it. The contact that most frequently automatically releases the occult punishing power is bodily contact. In many parts of Africa it is forbidden to touch anything from which the king or chief has eaten, be it the food or the plate from which it was taken. Anyone who willingly or unwittingly breaks this taboo is inescapably doomed to die, usually within a few days to a few weeks. So powerful is the force of suggestion here that the native who has broken the taboo often wastes away from no apparent cause.

The phenomenon of what has been called "voodoo death" is so interesting that a few words in explanation of the mechanism may be offered here. The evidence strongly suggests that death in such cases is due to the action of the sympathico-adrenal system in producing a marked decrease in blood pressure similar to that seen in wound shock. The blood volume is reduced until it becomes insufficient for the maintenance of an adequate circulation. Cannon¹⁹ writes

Thereupon deterioration occurs in the heart, and also in the nerve centers which hold the blood in moderate contraction. A vicious circle is thus established, the low blood pressure damages the very organs which are necessary for the maintenance of an adequate circulation, and as they are damaged they are less and less able to keep the blood circulating to an effective degree.

Constriction of the arterioles produces a dangerous fall in the oxygen supply of the capillaries of the

quence of the spiritistic beliefs that such peoples hold. Their ideas of causation may be wrong from our standpoint, or they may contain a grain of truth here and there, but given certain spiritistic concepts, the body of medical practice follows with a degree of consistency that we can only hope some day to equal. In short, it should be clear that, in his view of the nature of disease and its treatment, isolated man is no illogical unreasoning creature. He is, in fact, a thinker who, with the data at his disposal, does at least as well as we should do under similar circumstances. Let us, then, look on him with the respect and understanding that are his due.

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CLINICAL NOTE

URETERAL CATHETERIZATION

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STONEHAM, MASSACHUSETTS

FROM a discussion that was recently heard it is evident that a simple technic for catheterizing the ureters in the presence of a vesicovaginal fistula is not well known. I therefore call attention

to a method that was successfully used a number of years ago. Since the fistula was of moderately large size, it would have been impossible to distend the bladder enough for successful ureteral catheterization with the usual technic. The problem was solved by soldering a nasal atomizer tip over a flexible eustachian catheter, allowing the catheter to project slightly beyond the atomizer tip. The arrangement is seen in the accompanying illustration (Fig 1). No doubt the cannula used in the Rubin test would have served equally well.

The tip of the eustachian catheter was inserted

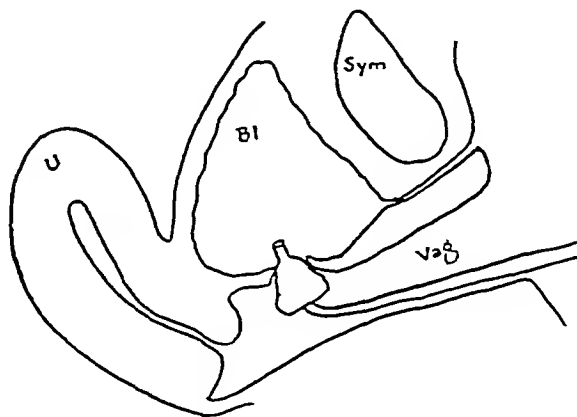


FIGURE 1

to a method that was successfully used a number of years ago.

It was desired to catheterize the ureters for their better identification during the closure of a high

through the vagina and fistula into the bladder. The atomizer tip thus occluded the fistula. The fluid passing through the eustachian catheter quickly dilated the bladder, allowing easy catheterization of the ureters.

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of rites such as naturally follow disease ascribed to the neglect of religious injunctions

Such minor ailments do not, therefore, necessarily fall into the domain of what would be called natural causation. Since they are unimportant, no one thinks enough of them to attribute them to any cause, and since they do not require any appeal to magical or spiritual agencies for cure, they are treated with domestic remedies

PRIMITIVE MEDICAL PRACTICE

A brief account of some of the more practical devices to which isolated man resorts in various parts of the world will serve to convey some idea of his ingenuity and the closeness of many of his practices to modern ones, or even their identity with them

Among the Ashanti of West Africa, inoculation for smallpox or against snakebite is successfully undertaken. In smallpox, the contents of a pustule are rubbed into an incision made in the skin. In the treatment for snakebite, the procedure is almost identical with the most recently devised methods. Veins are punctured by the use of splinters of stone or bone or by the use of a little arrow, which is shot into the vein from a miniature bow. Cupping and bloodletting are widely practiced, cupping is usually carried out by powerful suction with the mouth through a bone tube or similar instrument. Drainage from wounds is sometimes secured by means of sections of bamboo. Foreign bodies are extracted and abscesses opened with a thorn or a sharp-pointed instrument.

Suture or tight bandaging to promote union is not unknown among some tribes. Stitching of small wounds is carried out by means of thorns. A highly original method of suturing a wound is practiced among certain Indian tribes of Brazil. Both edges of the wound are allowed to be seized and brought together by the sharp head-nippers of certain ants, whose bodies are then rapidly cut off, one ant after another is used until the wound is closed.

Ulcers are frequently treated by cauterization with hot ashes or with heated blades and irons. In the treatment of fractured bones, splints and occasionally casts made of clay are used. On the whole, the results obtained by the native bonesetters are said to be extremely good. Trephining of the skull has already been mentioned. At all times a serious operation, this is skillfully performed by the native surgeon with a blade of stone or glass. There are skulls in museum collections that show that persons have been operated on in this manner as many as four or even five times. Evidence of healing around the bone edges shows that there has been good recovery in these cases.

Medicines are given in the form of decoctions, poultices, embrocations, salves and infusions of various sorts. Hydrotherapy, dietetics and massage

are widely practiced. Enemas are administered by means of primitive appliances, and fumigations, inhalations, snuffs, nasal douching and instillations are also more or less widely practiced. This list of medical practices could be widely extended, but enough has been said, it is hoped, to indicate that the medical resourcefulness of isolated man is scarcely less than our own.

A few words may be added concerning the medicine man. How does a person become a medicine man? The pattern varies with different peoples. In some tribes the position is hereditary, in others the addiction to epileptiform states is the best qualification, or a man may come to be recognized as possessing a special gift for setting broken bones. In still other tribes the would-be medicine man must undergo a special course of training, and in certain societies there are even distinct grades of medicine men—for example, among the central Australian aborigines. Here the three grades of medicine men are those who are made by the spirits, those who are made by a special class of mischievous spirits and those who are initiated by other medicine men. The first two grades are more highly regarded than is the third. In each case the man himself believes that he is especially capable of becoming a medicine man. Women may become medicine women in the same manner. Practically everywhere women are the midwives and child doctors. Among the American Indians one may become a medicine man in a variety of different ways. Among the central Algonquin peoples, for example, there still exists a secret society known as the Midewiwin. This society is the repository of most of the medical knowledge of the tribe—a sort of college of physicians—into which one may gain entry by apprenticeship in early youth or by payment of the necessary fees and acquisition of the proper knowledge at any later time. It is a great honor to be a graduate of the Midewiwin. Different degrees of medicine men are recognized, according to the type of initiation they have undergone, and there are different types of specialists in the various disorders to which man is heir.

In many other cultures a person becomes qualified to treat a disease by virtue of the fact that he himself has recovered from that disease. In Africa a man may become a doctor by apprenticing himself, for several years and at an appreciable fee, to an already established medicine man, who then teaches him what he should know. A graduate medicine man may go in for postgraduate work by purchasing still higher secrets from others whose practice has brought them great renown.

* * *

From this presentation of the concepts of disease held by isolated peoples it will be seen that their medicine represents a perfectly rational system. Their medical practices are a most logical conse-

coming seen in true idiopathic cardiospasm. Furthermore, the filling defect seen under the fluoroscope is not a true picture of the extent of the growth. The lesion may appear to be inoperable or questionably inoperable, yet actually be a relatively small carcinoma with extensive spasm.

Meyer and Kozoll⁵⁵ in an editorial on gastrostomy reviewed the records of 80 patients on whom gastrostomies were performed between 1941 and 1944. Forty-three patients died within two months of the performance of the gastrostomy. As these authors point out, such results speak for the futility of gastrostomy, even as a preliminary procedure, in resection of the esophagus.

I believe that most patients with carcinoma of the esophagus do not need a gastrostomy, either as a preliminary or a palliative procedure. A few of these cases can be determined to be inoperable by inspection of the liver with the peritoneoscope, and others are found to be inoperable at the time of exploratory thoracotomy. In those that are operable the problem of gastrostomy does not arise because the stomach is mobilized and anastomosed directly to the end of the esophagus. In those that are inoperable the patient's nutrition can in many cases be fairly well maintained by bougienage, with a previously swallowed thread used as a guide. Such patients are also given x-ray treatment.

In cases of carcinoma of the esophagus and in those of carcinoma of the stomach invading the cardia, Sweet⁵⁶ believes that direct inspection of the growth through the esophagoscope assists in making a correct diagnosis. A biopsy should always be obtained at such an examination and usually confirms the existence of carcinoma. The extent of the growth in the deep layers of the esophageal wall, however, cannot be determined by this method. Roentgen-ray visualization is of greater value for this purpose and gives more accurate information. Because of the frequency of direct invasion of the left main bronchus by the tumor in cases of carcinoma of the midesophagus, it is imperative to perform a bronchoscopy in all such cases. In this way an unnecessary exploration of the tumor through the chest may be avoided.

Benign Stricture

Clark and Adams⁵⁷ have reported 5 cases of trans-thoracic esophagogastrostomy for benign stricture of the lower esophagus. There were no deaths. In selected cases, trans-thoracic esophagogastrostomy offers the patient complete relief of symptoms without the necessity of repeated dilatations or the unpleasantness of a gastrostomy. None of the 5 patients were considered to have cardiospasm. In 1 case the stricture followed the ingestion of lye, in another it was associated with generalized scleroderma, and in 3 cases no etiologic factor could be ascertained.

Cardiospasm

Field⁵⁸ compares the effects of amyl nitrite, glyceryl trinitrate and octyl nitrite on achalasia of the cardia in 5 children. He reports that octyl nitrite relaxed the cardia and produced clinical improvement in 4 cases. The fifth patient failed to respond and on further investigation was found to be suffering from congenital stricture of the lower end of the esophagus. Field states that octyl nitrite is superior to amyl nitrite because its odor is pleasanter and less pungent than that of amyl nitrite, because it is less volatile and can thus be administered in an inhaler, which is a much more convenient form, and because clinically it produces relief and stops vomiting, whereas amyl nitrite often produces nausea and vomiting. The advantages of octyl nitrite over glyceryl trinitrate tablets or liquor glyceryl trinitrate are as follows: it is quicker in action, allowing less chance for food to be vomited, the necessary relief can easily be regulated by inhalations, according to the esophageal sensations felt by the patient, and clinically it produces relief and stops vomiting, whereas the vomiting continues under treatment with the other nitrites. The Octrite Inhaler* is a glass tube, with a vulcanite cap at each end, containing cellulose pellets impregnated with octyl nitrite. During use, both caps are removed and the inhaler is applied to one nostril, the other being closed. The author states: "The child now approaches his meals with the certainty that he can take them. No longer is he in fear that a heavy discomfort in the chest will bring eating to a stop, for he knows that this can be relieved without fuss by a sniff from the inhaler." The life of the inhaler tube varies from seven to twenty-eight days. The author further states that octyl nitrite inhalation also produced favorable results in adults suffering from cardiac achalasia.

Clagett, Moersch and Fischer⁵⁹ point out that the vast majority of patients who have cardiospasm obtain excellent results from dilatation of the cardia by means of the hydrostatic dilator, and that it is only in the exceptional case that surgical intervention becomes necessary. Approximately 70 per cent of these patients are completely relieved by one course of treatment. In 30 per cent of cases there is a tendency for the condition to recur. The recurrence may take place at any time from immediately after treatment to twenty-five years after it. If the condition does recur, the great majority of patients can be successfully relieved by subsequent dilatation. Dilatation of the esophagus by means of the hydrostatic dilator can be employed with little risk, in these authors' experience the risk having been less than 0.1 per cent. In 2 to 5 per cent of cases hydrostatic dilatation does not prove efficacious and surgical intervention is indicated. Of the surgical procedures that have been recom-

*Obtainable from Hynson, Westcott and Dunning Incorporated, Baltimore.

MEDICAL PROGRESS

ENDOSCOPY (Concluded)*

EDWARD B. BENEDICT, M.D. †

BOSTON

ESOPHAGOSCOPY

Benign Tumor

Adams and Hoover⁴⁵ report 3 cases of benign tumor of the esophagus and include a review of the literature. Many of these tumors were incidental discoveries at autopsy. The number of cases discovered and recorded during the last eleven years owing to good x-ray technic and esophagoscopy is over half as large as the number of cases recorded in the preceding two hundred and twenty years. In a pathological classification of these tumors there were 35 polyps, 10 myomas, 9 papillomas, 8 fibromas, 6 cysts and 5 or less each lipomas, adenomas and unclassified tumors. There were 1 aberrant thyroid gland, 1 benign giant-cell tumor, 1 hemangioma, 1 lipomyoma, 1 neurofibroma and 1 osteochondroma. In 2 of the cases reported by the authors the tumors were removed by open operation, the third was removed with the aid of a suspension laryngoscope after the tumor had been drawn into the oral cavity by means of an esophageal speculum.

Harper and Tiscenko⁴⁶ have discussed benign tumor of the esophagus and its differential diagnosis. Benign tumors are relatively rare as compared with malignant tumors. The case reported is that of a benign intrinsic extramucosal tumor of the esophagus in which the diagnosis was made roentgenologically by exclusion.

Carcinoma

Borges⁴⁵ analyzed 153 cases of cancer of the esophagus. Ninety-nine cases received esophagoscopic examination, and positive biopsies were obtained in 83. Distant metastasis was not the rule, the lymph nodes in the posterior mediastinum and those about the left gastric artery were the most frequently involved. The author believes in radical resection whenever possible.

Tomlinson and Wilson⁴⁶ have studied esophageal carcinoma in British West Indian and Panamanian Negroes. Although recent reports state that this tumor is far more frequent in white males, especially in those of Jewish extraction, than in West Indian and Panamanian Negroes, the authors found 50 cases in Negroes, Indians and mestizos. In 50 cases studied at autopsy, the periesophageal lymph nodes were grossly invaded in every case. In British West

Indian Negroes, carcinoma of the esophagus ranked third among all the types of carcinoma observed at autopsy.

Boros⁴⁷ states that carcinoma of the esophagus is one of the most frequent of all malignant diseases and is oftenest found in the male sex (75 per cent). Although his report, from the New York City Cancer Hospital, is extremely discouraging, the author mentions a glimmer of encouragement in the realm of radical surgery, referring in this connection to the work of Churchill and Sweet,⁴⁸ Wookey,⁴⁹ Garlock⁵⁰ and Ochsner and DeBakey.⁵¹

In an analysis of 599 cases of cancer, Toreson⁵² found 19 cases of secondary involvement of the esophagus, an incidence of 3.2 per cent, 14 of the tumors originating in the breast, 2 in the pancreas, and 1 each in the testes and mediastinal lymph nodes, in 1 case the origin was undetermined. In 12 cases sufficient esophageal obstruction occurred to cause clinical symptoms. From this analysis, it is evident that secondary carcinoma of the esophagus is not infrequent and that dysphagia occurs in about half the cases.

An unusual case of multiple carcinomas was reported by Holland⁵³ in a fifty-five-year-old woman. In 1933 she had an adenocarcinoma of the right breast removed, in 1939 a squamous-cell carcinoma of the esophagus and a small basal-cell carcinoma of the left cheek were treated by x-ray, and in 1942 an adenocarcinoma of the colon (Grade 2) was removed. Incidentally, in 1943, she developed a mild diabetes and had a cholecystectomy for cholelithiasis. At the time of the report, twenty-eight months after removal of the fourth carcinoma, the patient was without physical or roentgen-ray evidence of any malignant disease. The author states that this is one of the first recorded cases of carcinoma of the esophagus with a five-year cure following irradiation therapy.

In an article on the surgical treatment of some lesions of the lower esophagus and upper stomach, Bradshaw and O'Neill⁵⁴ call attention to the fact that it has been stated that a positive biopsy must be secured before the operation is undertaken and, of course, is highly desirable in all types of surgery. On the other hand, small lesions in certain localities at the cardia are not readily accessible to the esophagoscope, gastroscope or fluoroscope. A valuable aid in such cases is the occurrence of spasm of the lower esophagus, which does not present the smooth

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Case Records of the Massachusetts General Hospital In discussing this case Castleman,⁶⁵ the pathologist, stated his belief that the entire difficulty was related to the use of the gavage tube before the patient entered the hospital. The patient was the first of twins born seven weeks prematurely. The birth weight was 3 pounds, 1 ounce. The other twin weighed 2 pounds. Both children vomited frequently, and the other child died after one week. The patient was fed human milk by gavage many times while in the hospital. In the clinical discussion Farber⁶⁶ noted that gavage feeding of premature babies is frequently a necessity and saves many lives. It may be the cause of ulceration of the esophagus, however, particularly when the feedings are performed by inexperienced people. Such ulceration may form the starting point for infection, which may end in bacteremia. Pathologically, it was believed that the pulmonary lesions were almost certainly due to aspiration of the vomitus, which must have been mostly milk. It is also possible that at times some of the food fed by the gavage tube slipped down the larynx.

Rankin⁶⁶ reports a perforated ulcer of the esophagus following a burn. In 1842, Curling first described as a clinical entity an ulcer of the duodenum following a burn. To this day the etiology remains unknown.

The most popular theories for ulcer following burn are those of action of a burn toxin, stasis due to blood concentration, stasis due to low blood volume and adrenal activity, the embolic theory, the septic theory, the hypothalamus theory, the autonomic theory and the theory of nutritional disturbance. These ulcers are extremely rare, occur most frequently in children, perhaps reflect a severe toxemia, are seldom recognized during life and in general are an enigma in the medical literature. A case of perforated so-called "Curling's ulcer" of the esophagus with hemorrhage is reported. This occurred in a boy aged four years who had received second-degree burns to his thighs, buttocks and abdomen two days before admission to a hospital and died a few hours after it. Although none of these cases have been treated surgically, the only hope for the patient lies in immediate operation.

Smithers⁶⁷ has made a study of short esophagus (thoracic stomach) and its association with peptic ulceration and cancer. He first gives a historical sketch of congenital short esophagus and then discusses the theories regarding the association of thoracic stomach with peptic ulceration of the esophagus. Finding objections to the theories of congenital short esophagus and of fibrosis and constriction, he puts forward his own theory as follows:

Congenitally short oesophagus is rare, being seldom found at autopsy. Many cases so diagnosed during life have an acquired or an apparent shortening, rarely demonstrable after death, and resulting from hiatus insufficiency, sometimes developmental, more often acquired in later life. With the cardiac sphincter in the

thorax, released from any diaphragmatic control, gastric juice tends to flow into the oesophagus predisposing to peptic ulceration. Irritation of the oesophageal mucosa by gastric juice (or probably by oesophagitis from any cause) may produce irregular spasmodic contraction of the lower end of the oesophagus, which frequently appears, not only as irregular constrictions from side to side, but as longitudinal contraction or shortening. Relaxation of contraction and equalisation of pressure in the thorax and abdomen returns the herniated portion of the stomach to the abdomen by the time that a post-mortem examination is performed in cases where the oesophagus is of normal length. Heterotopic gastric mucosa may secrete gastric juice into the oesophagus or the gastric contents may reach it in other ways (for example, as the result of vomiting, rumination, or relaxation of the cardia following operations) in patients without a lax hiatus. Peptic ulceration of the oesophagus may occur in these patients without radiological evidence of shortening of the oesophagus. This theory (hiatus insufficiency, congenital or acquired, first, spasmodic shortening of oesophagus and ulcer, second) accounts for the known facts and overcomes the chief difficulties associated with the "congenital short oesophagus" and "fibrosis and contraction" theories. A new explanation of the shortening of the oesophagus, so real to the radiologist and often apparent at oesophagoscopy, but so little known to the pathologist, seemed to be required. An upward spasmodic contraction of the longitudinal fibres of the oesophagus during life, with relaxation after death, has been implied as a possible explanation in the theory put forward above. It seems possible that irritation which will produce oesophagitis or peptic ulceration of the oesophagus and irregular contraction of its lower portion may result in sufficient spasmodic contraction of the longitudinal fibres to produce apparent shortening and to retain a portion of the stomach in the thorax during life.

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mended, the authors prefer esophagogastrostomy performed through a transabdominal approach. A review of the literature and the authors' results indicate that this is a safe procedure that accomplishes good results. Although good functional results are obtained, one should not expect retrogression in size of the dilated esophagus after the operation.

I believe that the value of surgical procedures for cardiospasm is still unproved. Sometimes the results are not satisfactory, especially when operation is undertaken without an adequate trial of dilatation with the mercury bougie or with the hydrostatic dilator in experienced hands.

Scott⁶⁰ has analyzed 85 cases of idiopathic dilatation of the esophagus—usually diagnosed as achalasia of the cardia or as cardiospasm. Aided by the information obtained from the use of spinal anesthesia as a tool of investigation, he believes that it is possible to recognize four different clinical types, which probably also differ from each other in their etiology. These types are achalasia of the esophagus, true cardiospasm, dilatation associated with a constriction at or just above the cardia and dolichoesophagus. In conclusion, Scott states that achalasia is probably the most frequent type. It usually responds well to dilatation. In true cardiospasm the reflex originating focus should be discovered and removed. Those cases caused by a partial constricting band near the cardia are few in number but are probably resistant to conservative treatment. Dolichoesophagus—an S-shaped lengthening with pooling of esophageal contents at different levels—should probably be operated on immediately on recognition. This type is extremely difficult to control when the dilatation becomes gigantic and is complicated by infection of the esophageal wall. Subdiaphragmatic esophagogastrostomy—of the Finney pyloroplasty type—appears to be the operation of choice in those cases of idiopathic dilatation of the esophagus that are resistant to the usual conservative measures. The symptomatic results of this operation are usually excellent, whether or not the dilatation of the esophagus is entirely corrected. The danger of the operation is not excessive when proper precautions are taken. After it has been employed more extensively, the number of cases in which it is indicated will probably be considerably increased, but it should never replace conservative dilatation in the majority of cases.

Weens⁶¹ calls attention to the frequent association of pulmonary disease with megaesophagus. In 3 cases the respiratory symptoms had completely overshadowed the digestive disturbances so that the presence of the megaesophagus was almost missed. It is this author's opinion that the pulmonary complications in megaesophagus are the result of aspiration into the bronchial tree of food

particles regurgitated from the esophagus into the pharynx, as is so often noted in this condition.

Hawes and Soule⁶² have reported 2 cases of severe cardiospasm associated with extensive pulmonary changes. One patient, a man aged fifty-seven, showed an interstitial fibrosis with cough and hemoptysis, the other, a man of thirty-one, manifested an increased density in the right upper lobe. The authors mention that patients with cardiospasm are often bothered with coughing and occasionally sudden paroxysms of strangulation, which are frequently precipitated by lying down. In the recumbent position the large reservoir of food and fluid may spill into the pharynx and be aspirated, and the patient may be aroused from his sleep by severe coughing. At times, the fluid entering the bronchi leads to pulmonary disease. Five types of pulmonary changes associated with cardiospasm have been observed roentgenologically—basal pneumonitis, lung abscess, bronchiectasis, pleural effusion and interstitial pulmonary fibrosis. In each of the 2 cases reported there was a long-standing asymptomatic pulmonary lesion, probably an interstitial fibrosis following aspirating pneumonitis.

Bird-Acosta⁶³ also calls attention to pulmonary suppuration as a result of esophageal overflow. Esophageal retention may be caused by carcinoma of the esophagus, strictures, foreign bodies, pulsion diverticulum, extrinsic esophageal pressure from adjacent tumors and cardiospasm. Of all the causes of pulmonary suppuration following esophageal overflow, cardiospasm, although a fairly common clinical entity, is rarely considered. The author reports 3 cases of pulmonary suppuration as a result of cardiospasm.

Cardioesophageal Relaxation

A case of cardioesophageal relaxation is presented by Berk.⁶⁴ It was diagnosed by roentgen ray examination and confirmed by esophagoscopy. Cardioesophageal relaxation, or insufficiency of the cardia, is an abnormality of unknown etiology in which gastric contents regurgitate passively into the esophagus through a patulous cardiac sphincter. It may be looked on as the direct antithesis of achalasia (cardiospasm). In this case careful x-ray studies were carried out in which it was concluded that there was no herniation of the stomach but simply a relaxation of the cardioesophageal junction. Esophagoscopy disclosed the esophagus to be dilated and flabby. No true hiatus hernia was seen, and no gastric mucosa. The impression of the esophagoscopist was insufficiency of the cardiac sphincter. The chief symptoms of this disease are epigastric distress and a lumpy sensation at the lower sternum.

Ulcer

The case of a thirteen-week-old male infant with traumatic esophageal ulcer has been reported in the

Case Records of the Massachusetts General Hospital In discussing this case Castleman,⁶⁵ the pathologist, stated his belief that the entire difficulty was related to the use of the gavage tube before the patient entered the hospital. The patient was the first of twins born seven weeks prematurely. The birth weight was 3 pounds, 1 ounce. The other twin weighed 2 pounds. Both children vomited frequently, and the other child died after one week. The patient was fed human milk by gavage many times while in the hospital. In the clinical discussion Farber⁶⁶ noted that gavage feeding of premature babies is frequently a necessity and saves many lives. It may be the cause of ulceration of the esophagus, however, particularly when the feedings are performed by inexperienced people. Such ulceration may form the starting point for infection, which may end in bacteremia. Pathologically, it was believed that the pulmonary lesions were almost certainly due to aspiration of the vomitus, which must have been mostly milk. It is also possible that at times some of the food fed by the gavage tube slipped down the larynx.

Rankin⁶⁶ reports a perforated ulcer of the esophagus following a burn. In 1842, Curling first described as a clinical entity an ulcer of the duodenum following a burn. To this day the etiology remains unknown.

The most popular theories for ulcer following burn are those of action of a burn toxin, stasis due to blood concentration, stasis due to low blood volume and adrenal activity, the embolic theory, the septic theory, the hypothalamus theory, the autonomic theory and the theory of nutritional disturbance. These ulcers are extremely rare, occur most frequently in children, perhaps reflect a severe toxemia, are seldom recognized during life and in general are an enigma in the medical literature. A case of perforated so-called "Curling's ulcer" of the esophagus with hemorrhage is reported. This occurred in a boy aged four years who had received second-degree burns to his thighs, buttocks and abdomen two days before admission to a hospital and died a few hours after it. Although none of these cases have been treated surgically, the only hope for the patient lies in immediate operation.

Smithers⁶⁷ has made a study of short esophagus (thoracic stomach) and its association with peptic ulceration and cancer. He first gives a historical sketch of congenital short esophagus and then discusses the theories regarding the association of thoracic stomach with peptic ulceration of the esophagus. Finding objections to the theories of congenital short esophagus and of fibrosis and constriction, he puts forward his own theory as follows:

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Blakemore have carried out vein anastomoses in 10 cases, half consisting of uniting the splenic vein and the left renal vein after removing the spleen and left kidney. In 5 other patients they have anastomosed the portal vein to the inferior vena cava. Whipple states that these procedures are as yet purely experimental. He quotes Blalock⁷⁰ as having performed splenorenal vein anastomoses for portal hypertension in 4 cases, in 2 of which there was a disappearance of ascites and remarkable improvement. On the other hand, Blalock's enthusiasm is somewhat curbed because the other 2 patients have died since operation from recurrent bleeding from esophageal varices.

In a description of the technic of using vitallium tubes in establishing portacaval shunts, Blakemore and Lord⁷¹ state in conclusion

Every one of the 10 cases of portacaval shunts went through a successful postoperative convalescence. The interval following operation has been too short in some to judge the results. However, in 6 of the 10 cases the improvement has already been so outstanding as to justify continuing the procedure. The Eck fistula operation is better tolerated by the patient, probably because of less blood loss during the procedure.

Lye Stricture

For esophageal poisoning due to lye Crowe⁷² believes in the Bokay prophylactic therapy, using a No. 10 Fr. eyeless catheter filled with lead or mercury and tied off at the open end. It should be wet with water or a lubricating jelly, gently passed down the esophagus and left in place for five minutes daily, starting on the third day after the patient has swallowed the lye. The size of the catheter should be increased until difficulty is encountered in passing it.

Pellagra

Fisher⁷³ discusses the findings in 17 patients ill with pellagra, all of whom had a characteristic glossitis. Marked dysphagia was frequent. Esophagoscopy revealed an intensive hyperemia and in some cases edematous mucosa. Multiple tiny ulcerations of the esophageal mucosa were noted in 9 cases. Barium studies of the esophagus in 8 cases showed many small, constricted areas along its course. Following the daily administration of 150 mg. of nicotinamide, 15 mg. of thiamin chloride and 15 mg. of riboflavin, the patients could swallow solid food without experiencing dysphagia in from three weeks to two months. There was progressive improvement in the objective findings and clinical symptoms.

Foreign Body

Richardson⁷⁴ reports 17 cases of esophageal obstruction due to impacted meat. Twelve of the patients had no teeth of their own, and several of the others had very poor teeth. Six patients had a normal esophagus, but the other 11 had a narrowing

or constriction of some portion. Spontaneous recovery can occur but is rare. Esophagoscopy may not be necessary if caroid or papain is used in a 5 per cent solution to dissolve the impacted meat.

Fistula

Abbott,⁷⁵ in an article on abnormal esophageal communications and their types, diagnosis and therapy, concludes that abnormal fistulous communications may occur from the esophagus into the bronchial tree, pleural cavity, mediastinum, pericardium and more remote tissue spaces. An esophageal fistula presents a serious hazard to the patient's life but not necessarily a hopeless one. This report adds 6 permanent closures to the 15 previously recorded. A review of the literature and a description of 23 additional cases is given. Two unusual cases of esophagopericardial fistulas are included in these reports. Another case, in which a fistula between the esophagus and the trachea occurred in association with Hodgkin's disease, is described, and this communication was successfully treated. To Abbott's knowledge, no previous similar cases have been reported. The symptomatology and diagnostic methods are described. The management of an esophageal fistula demands acute interest in methods of the patient's nutrition and the employment of early adequate drainage. Some fistulas close spontaneously under this regimen alone. Direct surgical attack on esophageal fistulas is applicable in some cases but can sometimes be obviated by endoscopic topical applications.

Abbott has reviewed 22 cases of abnormal esophageal communication that have been handled at the Barnes Hospital. The predominating cause was found to be malignant lesions of the esophagus or larynx. These constituted 13 of the 22 cases reported, and another case occurred in association with Hodgkin's disease. Two fistulas were secondary to chronic empyema, 2 were secondary to operative procedures, and 2 were associated with syphilitic aortic aneurysms. One patient developed a fistula following instrumentation, and another developed one in association with a congenital diverticulum of the esophagus, instrumentation having been used in this patient. No examples of fistulas in relation to tuberculous empyema or tuberculous mediastinal lymphadenitis are contained in this report. This is due, at least in part, to the fact that patients with chronic tuberculosis are usually relegated to sanatoriums. The diagnostic measure of the greatest value consists of x-ray visualization of the fistula, preferably with iodized oil to prevent barium irritation of the lung parenchyma. Considerable difficulty may be encountered in trying to visualize these communications directly with the aid of the esophagoscope, but the instillation of methylene blue within the esophageal lumen followed by bronchoscopic examination can be a helpful measure.

Moersch and Tinnev⁷⁶ have found that the most frequent site of acquired fistula between the esophagus and the trachea or bronchi is at or just above the bifurcation of the trachea. The left main bronchus is involved oftener than the right. Carcinoma of the esophagus was found to be the most frequent cause of this type of fistula, accounting for 36 per cent of 39 cases. Rarer causes were trauma, syphilis, tuberculosis and esophageal diverticulum, with a number of causes responsible for single cases. The etiology was unknown, however, in several cases. The clinical findings were found to depend on the primary pathologic changes and the size and location of the sinus tract. In esophageal cancer, the development of the fistula is suggested when, after a period of dysphagia, the ingestion of food is followed by cough, expectoration and dyspnea. This occurs particularly after taking liquids. X-ray study after the ingestion of iodized oil usually demonstrates the lesion. Because of the nature of the underlying disease, the prognosis is usually poor, and the cancer itself or pneumonia or mediastinal or lung abscess causes death. Small fistulas due to trauma may, however, last for years. In these cases surgical repair may be of value.

Haight⁷⁷ has presented the anatomic and surgical problems concerned with the correction of congenital atresia of the esophagus with tracheoesophageal fistula. Reconstruction of esophageal continuity by a single-stage operation consisting of an extrapleural closure of the tracheoesophageal fistula and an anastomosis of the esophageal segments offers the most satisfactory approach to the correction of the anomaly. A primary anastomosis of the upper and lower esophageal segments was done in 16 of the 24 patients on whom an exploration was undertaken. Six of the 16 patients for whom an anastomosis was performed were living seven months to three years and one month after operation, and the reconstructed esophagus was patent in all cases.

GASTROSCOPY

Complications

Fletcher and Jones⁷⁸ report on the risks of gastroscopy with the flexible gastroscope, having had 2 fatalities in twenty-eight hundred gastroscopic examinations. In both cases the Herman Taylor gastroscope was used. This gastroscope has a longer rigid and shorter flexible portion than the Wolf-Schindler flexible gastroscope. Both these fatalities were believed to be due to an error in judgment. In the first case, gastroscopy was probably contraindicated, since the patient's tissues might have been expected to be in a fragile state as a result of recent scurvy. In the second case, extra pressure was exerted when the tip of the gastroscope was lying in the hypopharynx, such pressure should not have been applied. In addition to their own cases, Fletcher and Jones have heard of 5 other fatal cases.

The Herman Taylor gastroscope was used in 5 of these 7 fatal cases. The authors call attention to the fact that gastroscopy with the flexible gastroscope is proving to be an indispensable means of diagnosis in diseases of the stomach and is rapidly becoming a routine procedure in almost every large hospital in the country. It is inevitable that many gastroscopies should be performed by inexperienced gastroscopists. They believe that beginners have a false sense of security in their use of the instrument, based on the rarity of reported accidents. It is important that all users of the flexible gastroscope should realize that there is a slight but definite risk associated with the passage of the instrument, and that in this, as in all endoscopic methods, the greatest circumspection is needed. These authors believe the main risk is that of perforation of the upper part of the esophagus and the hypopharynx. Both their deaths occurred in elderly women. They admit that the flexible part of the Herman Taylor gastroscope is 2 mm wider and is appreciably stiffer than the corresponding part of the Wolf-Schindler apparatus and that extra care may be necessary for its passage into the esophagus. On the other hand, they believe that the Herman Taylor model gives a better view of the stomach than can be obtained with the Wolf-Schindler instrument, and they consider it the gastroscope of choice provided it is passed with care.

Schindler⁷⁹ reports a case in which an apparent rupture of the stomach occurred during gastroscopy and pneumoperitoneum developed. At operation three hours later no trace of a lesion was found, although the pneumoperitoneum was present. The patient recovered.

Gastroscopic Study

According to Renshaw,⁸⁰ the diagnostic study of many patients cannot be considered adequate and complete without gastroscopy, which is an office procedure. Contraindications for examination are chiefly diseases of the esophagus and mediastinum. The limitations of gastroscopy are few, the main one being the so-called "blind areas" of the stomach, which vary in size. The procedure is indicated in further study of patients with negative roentgenologic findings in whom gastric disease is suspected, for classification of many cases with indeterminate, suspicious or inconclusive roentgenologic findings and for elucidation of certain obscure conditions, such as unexplained gross hemorrhage and gastrointestinal allergy. Gastroscopy in combination with roentgenoscopy and study of gastric content removed by the fractional method of gastric analysis has made the diagnosis of organic disease of the stomach comparatively simple.

Hardt, Hufford and Raben⁸¹ have made an analytical survey of patients examined gastroscopically and roentgenologically. One or more gastroscopic and roentgenologic examinations were performed

in 1132 patients who complained of symptoms suggesting the presence of gastroduodenal disease. The facts provided by the two methods were compared. The evidence conclusively demonstrates that gastroscopy should be performed before a definite diagnosis of normality can be made, since these authors' experience indicated that the gastroscope is the most efficient diagnostic aid in making a negative gastric diagnosis and in diagnosing all types of gastritis. In their experience, gastroscopy was superior to roentgenography in the diagnosis of all types of gastric ulcer, including marginal ulcers. The gastroscopist was correct in 89 per cent of all types of benign ulcerating lesions, and the roentgenologist correct in 58 per cent. The final stages of healing of the ulcer can be followed only by means of the gastroscope. Gastroscopy likewise is more accurate than roentgenography in localizing the ulcer and can detect earlier any changes suggesting malignancy. Some type of chronic gastritis was diagnosed gastroscopically in 19 per cent of 239 patients with duodenal ulcer, and gastroscopy thus added an important secondary diagnosis otherwise unobtainable. Gastric carcinoma was recognized gastroscopically in 94 per cent of the patients and by roentgenograms in 79 per cent, with a combination of both methods the lesion was detected in 98 per cent. Incomplete diagnosis gastroscopically occurred in 5 per cent, and the diagnosis had to rest entirely on the x-ray findings. On the basis of the authors' experience, gastroscopy is indicated in all cases of persistent or recurrent gastric complaints with negative roentgenologic findings in which the clinician still suspects the presence of gastric disease, in many cases of proved gastric ulcer in which operation is not performed but in which the lesion should be watched from time to time not only roentgenologically but gastroscopically, in cases in which the x-ray findings indicate a suspicious gastric lesion or in which a definite diagnosis cannot be made roentgenologically, and in all gastric carcinomas except those located at the cardia or well advanced in their course.

In 2 patients with negative gastrointestinal x-ray examination and negative gastroscopy, Hufford and Stonehouse³² took roentgenograms of the Cameron-Schindler flexible gastroscope in the esophagus passing through the cardia and in various positions in the stomach. The degree of flexion of the gastroscope was greatest in the esophagus, and was of a lesser degree in the fundus of the stomach just below the cardia. The flexible rubber tip of the gastroscope flexes acutely to the left and slightly forward as it passes through the hiatus esophagus into the cardia. The blind spots in the gastric wall are the parts that are in contact with or short of the focusing distance from the objective or inclined away at such an oblique angle that only a darkened area can be seen. The action of this gastroscope as recorded by the roentgenograms is shown to be

sufficiently flexible to pass through the normal anatomical channels without any undue stress or strain. The air inflated into the stomach during gastroscopic examination casts an identifiable shadow on the roentgenograms and unless eructated flows freely from the stomach through the pylorus, which shows satisfactorily the antral end of the stomach with peristaltic waves and a fairly good duodenal bulb. This report is well illustrated by eight roentgenograms.

From the beginning of World War II until December, 1943, Tanner³³ performed twenty-two hundred gastroscopic examinations on 1738 patients. In his clinic, the main use of gastroscopy was for diagnosis and observation of gastric ulcer. Of 631 cases of gastric ulcer, 159 were diagnosed solely by gastroscopy, since they apparently yielded normal x-ray findings. There are several reasons for the difficulty in diagnosis of many of the gastric ulcers by x-ray. For example, an acute ulcer may be too shallow to retain barium, or after a hemorrhage its base may be filled with blood clot, which prevents the entry of barium to the crater, or there may have been considerable delay after hemorrhage in x-ray examination of the patients, during which time the ulcer heals and the scarring may be missed roentgenologically. Thirty-nine of the patients with duodenal ulcer in this series also had a gastric ulcer, and cancer was also seen in 2 cases on which duodenal ulcer alone was suspected roentgenologically. Tanner agrees that even direct visualization of an excised ulcer of the stomach may not abide the truth as to its innocence or malignancy. Nevertheless, he writes, one is rarely in doubt after gastroscopic visualization, because vitality appears to accentuate the differences, and where such doubt exists a second inspection after ten days of medical treatment usually gives the clue. Certainly it is well worth while to examine gastroscopically every patient with an ulcer that is not healing rapidly under medical management. Superficial types of cancer may be missed roentgenologically. In this series there were 13 cases of cancer that had been considered benign or had not even been diagnosed roentgenologically.

Gastritis

Cutler and Walther³⁴ have reported on the significance of chronic gastritis in an Army general hospital, stating that a wide difference of opinion still exists on the clinical significance of the gastroscopic findings of chronic gastritis. They studied 333 soldiers. In conclusion they state

The gastroscopic surveys of asymptomatic subjects in this study and those by other workers have indicated that gastric mucosal changes can occur in symptom-free individuals. Notwithstanding, chronic gastritis is much more prevalent in the group of patients who do complain of chronic upper abdominal distress. In our series of such cases the incidence of chronic gastritis compares closely with the estimates of other workers previously cited. The frequent association of gastritis with duodenal

ulcer has again been corroborated in this study. The routinely uneventful response of these patients to an ulcer regimen does not militate against the symptomatic significance of chronic gastritis for the ulcer syndrome may be mimicked rather closely by patients who have chronic gastritis alone. Apart from the hypertrophic group simulating peptic ulcer a large group of patients with chronic gastritis show no uniform symptom complex. Because of the frequency of associated complaints unrelated to the patient's gastrointestinal system it is difficult to believe that a chronic gastritis can alone play the leading etiologic role. A sampling of consecutive cases of chronic gastritis has demonstrated the predominance of psychogenic factors. The possibility therefore arises that the gastric mucosa by its organic changes points to a more basic disturbance of psychiatric importance.

Holtermann and Mähre⁵⁵ in a discussion of gastritis state that gastritis was present in every case of duodenal ulcer and was generally more pronounced and diffused than in gastric ulcer. Gastroscopy is the most reliable diagnostic method and may likewise aid in classification. The gastritis may also be demonstrated roentgenologically. Better information will be obtained when small amounts of contrast medium are spread evenly over the mucosa. Negative roentgenologic findings do not exclude gastritis. Differential diagnosis between hypertrophic gastritis and superficial catarrh and atrophy should not be based on roentgenologic findings.

Hypertrophic Gastritis Simulating Tumor

Pollard and Cooper⁵⁶ made observations of 8 patients in whom stomach x-ray films revealed a filling defect similar to that seen in carcinoma. All the patients were men, and their ages ranged from twenty-two to sixty-five years. In all but 2 cases subjected to gastroscopy, the diagnosis of localized hypertrophic gastritis was established with reasonable certainty by this method of examination. The diagnosis of hypertrophic gastritis and the absence of neoplasm was confirmed in 7 cases by laparotomy and in 6 cases by histologic examination of removed tissue. Since early diagnosis and treatment are essential in the management of gastric neoplasm and operation may be contraindicated in cases of hypertrophic gastritis, it seems important that all these cases be examined gastroscopically before surgery is undertaken. Furthermore, it is perhaps wiser not to depend on a trial of conservative therapy to establish the diagnosis. Localized hypertrophic gastritis is capable of producing a filling defect in the stomach that is difficult to distinguish roentgenographically from that of carcinoma. The symptoms of hypertrophic gastritis may be indistinguishable from those of peptic ulcer or gastric carcinoma. Neither roentgen-ray nor gastroscopic findings are enough in themselves to enable one to distinguish between localized hypertrophic gastritis of the lower regions of the stomach and annular neoplasm in that area.

Hinkel⁵⁷ has reported an interesting case of a localized hypertrophic gastritis simulating the roentgen-ray picture of a tumor. His case revealed

a neoplastic type of filling defect on the lesser curvature of the cardia of the stomach. The tumor-like filling defect was also demonstrated, following pneumogastry, as a soft-tissue mass protruding into the gas bubble. The author discusses the differential diagnosis and briefly cites some of the literature on this subject. He points out that the protruding mass of the pseudotumor is due to a piling up and crowding of the hypertrophic redundant inflammatory mucosa. He emphasizes that achlorhydria is strikingly frequent in this form of gastritis.

Postoperative Gastritis

Browne and McHardy⁵⁸ limit their discussion to chronic postoperative gastritis. They point out the difficulty of a clinical diagnosis following gastrectomy, since this type of gastritis may mimic many gastroenteric lesions. Gastroscopy is suggested. Subclassification is limited to superficial, hypertrophic and rarely atrophic gastritis. The degree of redness of the mucosa was related to the hematopoietic status of the patient. A combination of the first two classifications was frequently encountered, it was severer in the anastomotic area, extending even into the jejunum. An accurate description of the findings is given. Causative factors such as chronic illness, severe trauma, achlorhydria and improper dietary regulations are given instead of the bacteriological factors. The authors give an optimistic prognosis, and after finding roentgen-ray therapy unsatisfactory, they suggest an ulcer regime supplemented by vitamins and liver extract. A case is reported.

Christiansen⁵⁹ believes that postoperative gastritis is a special form of gastritis, differing from other forms in its clinical picture as well as in its pathological and gastroscopic aspects. Gastroscopy reveals an extremely polymorphous picture, which is characterized by a mixture of superficial, hypertrophic, atrophic, erosive and ulcerative lesions. The clinical symptoms differ in many respects from those of peptic ulcer — for instance, the pain is not relieved by food intake. The question of pathogenesis is open to argument, and different theories are discussed.

Gastric Ulcer

Freeman⁶⁰ believes in the gastroscopic control of the treatment of gastric ulcer by duodenal feeding. Although roentgenography is still the standard method of choice in the diagnosis of an ulcer, this author has found a number of ulcers by gastroscopy that were missed by the radiologist, this may have been accounted for by failure of the barium to fill the crater because the floor was already filled with slough of mucus. Therefore, patients who present ulcer symptoms and in whom a negative x-ray examination has been reported should be examined with the gastroscope, and the examination should

be repeated subsequently before cessation of treatment is contemplated

Carcinoma

In commenting on the relation between diet and cancer, Grossman and Ivy⁹¹ raise the question of the possible relations between dietary irritants and gastritis and gastric cancer. They state

Cramer (1934) has observed that the total cancer rate is the same in England and Holland, though the incidence of cancer of the stomach in Holland is approximately twice as great as in England. A subsequent study of Lintott (1939) and Herbert and Bruske (1936) indicated that the Dutch people consume more roughage, hotter food and more spices, spirits and tobacco and have more oral sepsis than the English.

Stout⁹² has made a study of gastric mucosal atrophy and carcinoma of the stomach. This study revealed that mucosal atrophy may appear as early as the third decade and is found with increasing frequency and extent in the succeeding decades of life. In comparable groups of stomachs mucosal atrophy is found in a large number and tends to be more widespread in those with cancer than in those without it. But when one tries to find actual progression from altered mucosal glands, gastric or intestinal in type, cystic or not, distorted or regular, it is realized that it is impossible to tell when there is juxtaposition of carcinoma and mucosal gland, whether the carcinoma is invading the gland or developing from its epithelial cells. In occasional stomachs with carcinoma multiple sections from various areas failed to show epithelial changes in some, whereas others showed only minimal changes. Although atrophy of the gastric mucosal epithelium and cyst formation were present to a greater degree and in larger numbers in stomachs with carcinoma than in comparable stomachs without it, the exact relation between these conditions remained undetermined.

Dailey and Miller⁹³ in a search for symptomless gastric cancer in 500 apparently healthy men of forty-five and over conclude that a survey of the general population in search of gastric cancer is not worth while. Studies of selected groups such as those with pernicious anemia should be expanded, since this seems a profitable approach to the problem.

In a discussion of Krukenberg tumors, Lowman and Kushlan⁹⁴ emphasize the importance of a gastrointestinal survey in cases of ovarian malignancy to determine if possible a primary source of the tumor in the digestive tract. They stress the importance of using every available means of diagnosis in the differentiation of early carcinoma of the stomach and benign gastric ulcer—that is, serial roentgenographic studies and gastroscopy. Gastric ulcer not responding to therapy with rapid and complete healing as demonstrated by x-ray and gastroscopy should be treated as malignant and resected early.

Sweet⁹⁵ believes that the use of the gastroscope is of limited value in cases of carcinoma of the stomach near or invading the cardia. In an occasional case in which the roentgen-ray examination is equivocal, inspection through the gastroscope may help to establish a correct diagnosis.

In a careful analysis of the data available for a ten-year period at the Massachusetts General Hospital, Allen⁹⁶ has found that 14 per cent of the patients treated as having benign gastric ulcer proved to have cancer. These patients responded well to conservative therapy at first, with disappearance of symptoms and a regaining of lost weight. The lesion often appeared to diminish in size on roentgen-ray and gastroscopic examinations. Consequently, Allen is afraid of conservative treatment. He believes that early radical surgery is indicated when a patient appears for treatment with an ulcer of the stomach in the prepyloric or fundal regions. If he is over forty years of age and has had symptoms for less than one year or if his ulcer is over 2 cm. in diameter, the same advice should be given. If the patient is young and has a small lesion or if the ulcer is superimposed on symptoms of more than five years' duration, a more conservative attitude is justifiable. This patient should not be treated in an ambulatory fashion, as is the usual practice in mild or early duodenal ulcer, but should be given the benefit of an adequate hospital regimen. If the ulcer remains even partially unhealed after one month of such therapy or if there is a return of ulceration one month after healing is apparent, the patient should be urged to submit to surgery.

Since the advent of liver therapy, Olson and Heck⁹⁷ had found a notable increase in the number of cases of carcinoma and polyps of the stomach in cases of pernicious anemia. Undoubtedly it is significant that patients who have pernicious anemia now have an indefinite prolongation of life. The processes that are active in the alteration of the gastric mucosa are permitted by this extension of life to continue for many years. This factor is probably the one that is responsible for the increased incidence of polyps and carcinoma of the stomach. Pernicious anemia is a disease of the gastric mucosa as well as a disorder of the hematologic and neurologic systems. Treatment that is sufficient for the maintenance of normal blood may not be adequate to prevent atrophic changes in the gastric mucosa, which in pernicious anemia may not only become atrophic but may produce benign and malignant growths.

In a study of pernicious anemia and the early diagnosis of tumors of the stomach, Rigler, Kaplan and Fink⁹⁷ state that despite the expansion of roentgen-ray diagnosis, the more general use of gastroscopy and the refinement of the methods of examination of the gastric contents and stool, the record is a black one. The over-all salvage of only 2 per cent of the patients afflicted with this disease

or even the survival of 6 per cent, which is the maximum reported, gives a picture of the difficulties involved. The importance of gastroscopy is emphasized in the case of a patient with pernicious anemia and a benign polyp 4 mm in diameter not found on the first x-ray examination but discovered gastroscopically and later confirmed by x-ray. The possibility of the malignant degeneration of a polyp should be particularly brought to mind in cases of pernicious anemia because of the tendency of the latter to develop carcinoma. In 1939, Rigler, Kaplan and Fink⁹⁷ undertook to examine roentgenographically all their patients with pernicious anemia at semiannual intervals. In summary, they state that in a roentgen-ray study of 211 patients with pernicious anemia on whom examinations of the stomach were made on one or more occasions, carcinoma of the stomach was found in 8 per cent and benign polyps in 7 per cent. In an autopsy study, reported elsewhere,⁹⁸ 12 per cent of patients with pernicious anemia were found also to have carcinoma of the stomach. The data presented indicate clearly an etiologic rather than an accidental relation between pernicious anemia and tumors of the stomach. The routine roentgen-ray examination of the stomachs of patients with pernicious anemia has proved to be a valuable procedure resulting in the salvage of some cancer cases that might otherwise not have been saved. Cases were observed illustrating the rapid change from a benign polyp to a cancer, the presence of both benign and malignant tumors side by side, the absence of symptoms in the presence of large tumors and the development from a small, barely detectable lesion to an extensive, inoperable carcinoma.

In a recent editorial, Benedict⁹⁹ states that a more accurate diagnosis can be obtained in the problem of gastric ulcer and carcinoma when all methods of examination are used in a given case than when reliance is placed on incomplete data. Gastroscopic examination supplements x-ray examination, it does not in any sense compete with it. Reliance can be placed on gastroscopic examination only when the method is carried out by an experienced gastroscopist who knows the limitations of the method, the relative blind areas in the stomach and the proper interpretation of his observations. In a recent lecture, Benedict¹⁰⁰ reported his study of 245 proved cases of gastric disease in an attempt to correlate the gastroscopic, x-ray and pathological findings. An analysis was made of 125 cases of proved carcinoma of the stomach in which it was shown that x-ray and gastroscopic examination were equally good in 67 cases and equally doubtful in 3 cases. X-ray examination was more accurate or more helpful in 32 cases, and gastroscopy was more accurate or more helpful in 20 cases. When the lesion was equally accessible to both methods of examination, the analysis indicated the relative

superiority of gastroscopy over radiology in differentiating benign and malignant gastric ulcers. In the same report, 50 cases of proved benign gastric ulcer were analyzed. In 16 of these x-ray and gastroscopy were equally correct, in 9 cases they were equally doubtful, in 21 cases x-ray examination was superior to gastroscopy, and in only 4 cases gastroscopy was superior to x-ray. In both the carcinoma and the ulcer cases, gastroscopic failures were largely due to mechanical difficulties, which accounted for 25 of the 32 cases of x-ray superiority in the carcinoma group and for 17 of the 21 cases of x-ray superiority in the ulcer group. Benedict concludes that gastroscopy is of value in the ulcer-carcinoma problem and that the most accurate diagnostic results are obtained when all methods of study are used in combination.

Benign Tumor

According to Dewey,¹⁰¹ the incidence of benign tumors of the stomach is estimated at 0.5 to 5.0 per cent of all gastric neoplasms. Adenomatous polyps are seven times more frequent in association with atrophic gastritis than in the presence of a normal mucosa. Diagnosis depends on roentgenologic and gastroscopic study, but the final determination is made by histologic examination. Early surgery is the proper treatment.

Gastric Mucosa in Hepatitis

Knight and Cogswell¹⁰² examined by gastroscopy 9 patients with infectious hepatitis in 7 of whom the appearance of the mucosa was found to be abnormal. The area involved was always the anterior portion of the stomach, and in some cases the abnormal appearing areas extended into the fundus. The findings that have impressed these writers as being most distinctly abnormal gave the appearance through the gastroscope of being almost identical with the small aphthous ulcers that are often seen in the mouth. Five patients in this series were observed to have these ulcerations. Further study is essential before any conclusions can be formulated with regard to the relation between the findings in the gastric mucosa and infectious hepatitis.

Hemorrhage

From a study of 112 patients who had had gross bleeding from the upper gastrointestinal tract, Clark¹⁰³ advocates gastroscopic examination after hemorrhage of undetermined origin.

In an article on inflammatory lesions of the upper gastrointestinal tract, Aaron¹⁰⁴ suggests the following criteria for healing of ulcerated lesions of the stomach: complete cessation of all symptoms, maintenance of or gain in weight, persistent absence of occult blood from the feces, disappearance of anemia of the iron-deficiency and essential-factor type, a normal sedimentation rate, roentgenologic evidence of complete healing, and, if it is possible

to obtain it, confirmation by gastroscopy. Only when these studies are repeated over a four-week to six-week period of observation can one be sure that a lesion of the stomach has healed and remained healed and is thus likely to be benign. If this does not occur, the patient is entitled to surgical intervention.

Jankelson¹⁰⁵ has studied 60 cases of hematemesis of unexplained origin. Seven patients died before extensive studies could be carried out. In 3 of them, autopsy did not reveal the source of the bleeding. The other 53 patients had intensive posthemorrhage studies, including roentgen-ray examination in all cases and gastroscopy in 10 cases. In retrospect, Jankelson advocates earlier x-ray study as well as more frequent and earlier gastroscopic examination to demonstrate acute changes in the gastric mucosa, which often heal rapidly without leaving any permanent changes. Acute hemorrhagic gastritis, multiple fissures of the stomach and some gastric ulcers will thus be demonstrated.

Although 50 per cent of cases of chronic seasickness present x-ray evidence of hypersecretion, loss of gastric motility and spasm of the pylorus, as well as thickened gastric rugae in some, Benedict and Schwab¹⁰⁶ state that the gastroscopic picture is usually essentially normal.

PERITONEOSCOPY

- In a report from the Memorial Hospital in New York City, Narancio, Pierson, McNeer and Pack¹⁰⁷ state

Our chief interest in this endoscopic field has been in the determination or recognition of the inoperability of various intra-abdominal neoplasms. One can frequently appreciate the inoperability of some cancers by this examination, but, on the contrary, the resectability can never be ascertained with any degree of certainty. If this fact were universally known, the limitations of the instrument would be accepted and no extravagant claims for its use would be made. The chief indication for its use, in our hands, is the attempted determination of inoperability in borderline cases.

Boehme¹⁰⁸ believes that peritoneoscopy has a definite and valuable place in the field of endoscopy. The enthusiasm for peritoneoscopy varies directly with the skill of the operator. Thus, also, the information gained on examination depends greatly on the skill and experience of the operator. Biopsy of the spleen was performed with some trepidation in 1 case. Only slight hemorrhage was encountered, and this was controlled by cautery. Fibrin foam was held in readiness, and it was intended to apply it to the bleeding surface by introducing it in the jaws of the biopsy forceps. This procedure should add a safety factor to biopsy of the spleen in the future. The indications for the use of peritoneoscopy to complete abdominal diagnosis are discussed. It is a safe, brief, relatively painless and valuable procedure. The anatomical and other limitations are reviewed to aid in careful selection of cases for examination.

Sweet⁵⁶ believes that the use of the peritoneoscope does not assist in the determination of the resectability of a local growth in the cardia or fundus of the stomach. In many such cases the tumor can not be visualized by this means, but when liver involvement or abdominal carcinomatosis is suspected, peritoneoscopy should be carried out so as to avoid performing a major exploration in inoperable cases.

From a study of primary tumor of the liver, Warvi¹⁰⁹ concludes that biopsy is imperative. Peritoneoscopy offers some opportunity to determine operability in addition to obtaining a specimen for microscopic study. Resection of primary tumors of the liver may be indicated in adenomas, cystadenomas, localized solitary carcinomas and hemangiomas, with certain restrictions.

In a recent Cabot case record of the Massachusetts General Hospital¹¹⁰ the value of peritoneoscopy in acute pancreatitis was demonstrated. During the peritoneoscopy the entire peritoneum, anterior gastric wall, small bowel and liver were seen to be covered with small, pale-yellowish implants averaging 2 mm in diameter. Biopsy of one of these implants showed fat necrosis.

Volwiler¹¹¹ believes that under certain conditions in diffuse disease of the liver, aspiration biopsy¹¹² has proved highly satisfactory in diagnosis. When properly used it is easier than peritoneoscopy, but of course the site of selection of the tissue cannot be determined under direct vision. It has the advantage of being a simpler procedure than peritoneoscopy and also of securing a biopsy specimen from deep in the parenchyma of the liver. When carcinoma is suspected, a direct inspection should be made by peritoneoscopy.

Decker and Cherry¹¹³ have found culdoscopy, or the endoscopic visualization of the pelvic organs by the vaginal route, superior to peritoneoscopy in the diagnosis of pelvic disease and in physiologic study. They believe that the procedure is invaluable in the investigation of pelvic tumors, ovarian disease, endometriosis and ectopic pregnancy and is especially helpful in the detailed study of primary and secondary sterility in women.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

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CASE 32281

PRESENTATION OF CASE

A fifty-nine-year-old Italian woman entered the hospital because of weakness and pain in both arms.

She was apparently well until twenty months before admission, when she had a pelvic operation the exact nature of which was not known, but which was done per vaginam and was apparently a repair of a cystocele. This operation was performed because of a burning sensation on urination. Two months later she developed pain in the left thigh and weakness of the legs, which tended to buckle under her when she climbed stairs. Ten months before entry the pain disappeared, but she noticed ankle swelling that gradually progressed up her legs. The weakness of the legs also progressed, and three months later she could no longer negotiate stairs without help and there was swelling up to the thighs. Two months later, she was seen at another hospital, where an x-ray examination of the chest, a gastrointestinal series, a barium enema, an intravenous pyelogram and peritoneoscopy were reported as negative. During her three-week stay in that hospital, the swelling of the legs decreased and continued to do so on a low-salt diet. She was discharged with a diagnosis of thrombophlebitis. Shortly afterward she began to have sharp pains in the calves and ankles that later progressed up to her hips, back and arms. She obtained some relief with heat and aspirin. At about the same time, she noted the onset of intermittent fever as high as 102°F, with such excessive sweating as to necessitate changing her bedclothes two or three times a night. She also had marked tremors in both hands. One month before entry the patient developed nocturia (three times) and also became anorexic. Her condition remained essentially unchanged until seven days before entry, when there was a sudden onset of pain in the arms, especially at the shoulders, elbows and wrists and in the neck, jaw and back of the head. Concomitantly she noticed marked weakness in both arms. During the year before admission she had lost about 25 pounds.

Her past history was noncontributory. She had borne eight children.

Physical examination revealed an ill appearing

woman who did not move her arms, was perspiring freely and was apparently in pain. The left pupil was larger than the right, but both reacted normally to light. A firm, nontender, 3-cm node was felt in the left axilla. There were dullness and absence of breath sounds at the right base. The liver edge was palpated three fingerbreadths below the costal margin, and a questionable mass was palpated below it. The vagina appeared constricted. No cervix or fundus could be felt. Examination of the arms revealed wasting of the deltoid and biceps muscles and absence of biceps and radial reflexes. The legs showed wasting of the quadriceps muscles, loss of knee and ankle jerks and moderate ankle edema. The only sensory changes were tenderness over the seventh cervical vertebra and over the anterior portion of the left mandible, with anesthesia of the left side of the chin, including the lower lip.

The temperature was 100°F, the pulse 120, and the respirations 24. The blood pressure was 155 systolic, 85 diastolic.

Examination of the blood showed a red-cell count of 4,200,000, a hemoglobin of 10.5 gm and a white-cell count of 7300, with 74 per cent neutrophils and no abnormal cells. Another observer noted the presence of occasional nucleated red cells. The serum phosphorus was 4.3 mg per 100 cc., and the alkaline phosphatase 5.3 Bodansky units. The non-protein nitrogen was 24 mg and the total protein 7.0 gm per 100 cc, with an albumin-globulin ratio of 1.3. The cephalin flocculation test was negative after twenty-four hours and \pm after forty-eight hours. A catheterized specimen of urine gave a +++ test for albumin, and the sediment contained up to 20 white cells per high-power field. The specific gravity of four specimens ranged from 1.012 to 1.022. Two stool specimens were formed, brown and guaiac negative. The spinal fluid was negative except for a protein of 125 mg and a sugar of 120 mg per 100 cc, and 1000 red cells per cubic millimeter.

X-ray examination revealed areas of increased density in the right lower chest, probably involving the middle and lower lobes and consistent with collapse (Fig 1). A small amount of fluid appeared to be present in the right pleural cavity. A plain film of the abdomen showed fixation of the right half of the diaphragm. It was not definite whether the area of density on the right side was above or below the diaphragm.

Despite supportive therapy the patient rapidly failed, becoming increasingly dyspneic and weak. She had constant diaphoresis. Thoracentesis was attempted between the sixth and seventh ribs posteriorly, but no fluid was obtained.

The patient died on the tenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR ALFRED O LUDWIG I should like to begin by looking at the x-ray films

DR. JAMES R. LINGLEY These films show the marked elevation of the right half of the diaphragm, with density in the lower lung field that is consistent with collapse of the lower lobe. There is probably a small amount of fluid in the costophrenic angle. The plain film of the abdomen shows a moderate amount of gas in the colon. There is a shadow beneath the lower border of the liver that could be a gallstone or calcification in a costal cartilage.

DR. LUDWIG Is that not a process in the lung?

DR. LINGLEY I believe that there is collapse of the lower lobe. The diaphragm is elevated, and the elevation could be due to subdiaphragmatic

diagnosis of thrombophlebitis was made. I do not see how anyone can say whether that was the correct diagnosis. It could have caused the symptoms that she presented. It is surprising that a swelling of the legs, supposedly due to circulatory obstruction, decreased on a low-salt diet. The next striking factor in this history is the onset of pains in the calves and ankles, with progression up to the hips. It is my impression that the pains were of neurologic rather than local origin. We know nothing about the condition of the joints at that time, and I think that we must assume that they were normal. About then she developed fever, which continued



FIGURE 1

disease or to collapse of the lung. The films do not help much on that. We also have a film of the cervical spine, which is negative.

DR. LUDWIG It seems to me that the outstanding episode in this woman's illness is the development of pain and increasing weakness of the legs two months before entry, associated at first with rather marked edema. She was studied extensively elsewhere, we do not know what was found, but the

until the time of death. It is necessary to explain the origin of that fever. The first thing to think of is infection, since this woman had a deep-seated thrombophlebitis. I also think of cancer, of which there are no clues, however. Cancer could also account for the fever. In that regard lymphoma should certainly be considered. The tremors I cannot explain, although they may have been due to weakness. There is no indication that this woman had any

acute cerebral accident The final and important part of the history is the sudden onset of pain in the arms, back of the head, various joints and jaw I should be interested to know exactly what the joints looked like

DR JOHN STANBURY The joints were normal

DR LUDWIG I assumed that they were Furthermore, arthritis or rheumatic fever could hardly have produced the picture described

The patient had nocturia, from which I judge that some renal insufficiency was present The history of anorexia and weight loss does not help much They are consistent with any chronic illness, whether due to cancer or to chronic infection The irregularity or the disproportion of the size of the pupils is not helpful to me, because there were no other pupillary abnormalities I should like to know, of course, what that firm, nontender 3-cm node in the left axilla was It seems a little large to be accepted as a normal lymph node The chest signs were not discussed by the roentgenologist, but he raised the question whether the trouble was above or below the diaphragm Judging by later statements in this history, one must certainly consider something above the diaphragm because of the marked dyspnea that developed The fact that the liver edge was three fingerbreadths below the costal margin is an important finding, as is the questionable mass palpated below it I forgot to ask Dr Lingley if he could see that mass in the x-ray film

DR LINGLEY I do not see any mass I think that the liver is enlarged

DR LUDWIG Is the enlargement an intrinsic increase in size, or is the liver depressed by something above it?

DR LINGLEY You can see the lower border fairly well from the splenic flexure of the colon, and the entire liver shadow looks rather large to me

DR LUDWIG The vaginal examination was normal The examination of the arms which showed wasting of the muscles and the absence of biceps and radial reflexes, must also be taken seriously Because of the absence of sensory changes, it seems to me that there must have been some disturbance in the anterior-horn cells or in the anterior roots Without any sensory abnormalities, I do not see how one can assume that this was due to peripheral neuritis or neuronitis The anesthesia on the left side of the chin, including the lower lip, is somewhat difficult to explain, and I believe that it was on the basis of some local interference of the roots of the fifth nerve going to that part of the face I think that the other important finding in the physical examination is the tenderness over the upper cervical vertebrae The wasting of the quadriceps muscle and the loss of knee and ankle jerks probably mean the same thing in the lower extremities as in the upper extremities, namely, that there was some interference in the anterior-horn cells or roots

The laboratory findings, so far as the blood is concerned, help me little There was a moderate degree of secondary anemia The serum phosphorus, the serum phosphatase and the total protein were within normal limits I am not disturbed by the cephalin flocculation test The +++ test for albumin was found in a catheterized specimen, and if it is to be taken seriously, it indicates some type of renal disease Four urine specimens had specific gravities ranging from 1.012 to 1.022 That means that she was still able to concentrate urine relatively well Nevertheless the albuminuria is indicative of renal disease The spinal-fluid findings are quite disturbing Certainly the protein was markedly elevated, the normal upper range being somewhere around 45 mg per 100 cc The sugar value was high, since the normal spinal-fluid sugar ranges from 60 to 70 mg per 100 cc I should like to know what the blood sugar was Incidentally, I cannot think of any neurologic condition that is characterized by an increase in the spinal-fluid sugar Usually such an elevation mirrors a concomitant elevation of the blood sugar Is there a record of the blood sugar?

DR TRACY B MALLORY No blood sugar was recorded

DR LUDWIG We shall have to throw out the finding of high sugar in the spinal fluid, I do not know what it means

I think that we can say definitely that the finding of 1000 red cells per cubic millimeter was not responsible for the 125 mg per 100 cc of protein I should like to know whether the cells were crenated, and whether they appeared immediately at the beginning of the test, or when the last portion of the spinal fluid was withdrawn

DR STANBURY The cells were not crenated and were in the last portion of the fluid

DR LUDWIG In the last phase of this case attention was focused on the right chest and unsuccessful attempts were made to withdraw some fluid, undoubtedly for diagnostic purposes

After putting all this together, the most honest answer is, I do not know-the diagnosis I believe that the woman had thrombophlebitis to begin with Could that have progressed to produce pyelphlebitis? Certainly there is no evidence of pyelphlebitis, which is usually associated with infection in the region of the appendix and is followed by an intermittent spiking temperature, multiple abscesses of the liver and jaundice, which usually runs a rapid course unless the infection is curtailed It is possible that there was an infection in the region of the liver If that were so, one of my guesses would be that there was a subdiaphragmatic abscess I cannot say, however, that there is much evidence of such an abscess Could this patient's symptoms be explained on the basis of multiple venous thromboses? I think that that is possible There is nothing to suggest that the difficulty in the lung was

due to a pulmonary embolus there was no hemolysis or history of chest pains, and no indication of endocarditis or cardiac valvular disease. Finally how can one explain what happened in the spinal canal? The patient could have had a thrombosis or embolus in the spinal canal. It would be extremely unlikely for either condition not to produce a definite myelitis, with a level and with sensory changes that were not present in this case. I have seen one case in this hospital in which there was a high spinal-fluid protein without block, which was due to a hemangioma. I gather that there was no block in the case under discussion. Hemangiomas of the spinal cord, which occur on the posterior surface of the cord, usually produce fairly marked sensory changes. Another possibility is an epidural abscess in the bony structures in the area of the seventh cervical vertebra, with some encroachment on the spinal cord. Whatever happened there apparently happened suddenly. Whether a small abscess rapidly increased in size, or burst or produced some local thrombosis, I do not know. In either event an abscess in the region of the seventh cervical vertebra was probably found. Again, I am quite at a loss to explain the terminal episode in this woman's illness. We are told that she failed rather rapidly, showed increasing dyspnea, and died. This may represent a terminal pneumonic infection, but from what we are given I can draw no conclusion. I do not know why she died.

In summary, although I do not believe that I am close to the diagnosis, I think that this woman had a chronic infection. It is possible that she had multiple septic venous thrombosis or multiple abscesses — one in the region of her liver, followed by a subdiaphragmatic abscess, and another in the region of the seventh cervical vertebra. Cancer is always possible, and cannot be ruled out in this case. If a biopsy on the axillary lymph nodes had been done, much light would have been shed on this case.

DR MALLORY: I think that you should have some additional information, Dr Ludwig.

DR LUDWIG: I do too.

DR MALLORY: A biopsy of the axillary lymph node was made, but the answer was not available at the time the patient died.

A PHYSICIAN: Was a test for Bence-Jones protein done on the urine?

ANOTHER PHYSICIAN: The urine was examined for Bence-Jones protein and was negative.

CLINICAL DIAGNOSIS

Malignant lymphoma

DR LUDWIG'S DIAGNOSIS

Multiple septic thrombophlebitis, with secondary abscess formation (in region of liver and epidurally in cervical region)?

Malignant tumor (origin and type unknown)?

ANATOMICAL DIAGNOSES

Malignant lymphoma involving retroperitoneal tissues and meninges of spinal cord.

Thrombosis of right hepatic vein

Thrombophlebitis of iliac vein, old

PATHOLOGICAL DISCUSSION

DR MALLORY: Our first opinion in the laboratory was that the lymph node removed showed simple hyperplasia. On reconsideration we eventually decided that the diagnosis was giant follicular lymphoma. Autopsy showed an extensive retroperitoneal lymphoma involving the mesentery and the tissues around both kidneys. Histologically this also proved to be lymphomatous but showed no traces of follicle formation. The elevation of the diaphragm on the right must have been largely due to tumor around the right kidney. The liver was enlarged, not because of the few small foci of tumor but because of a thrombosis of the right hepatic vein, with a partial infarction of the entire right lobe of the liver. The spinal cord seemed at first negative, but on more careful examination the meninges were found to be focally infiltrated with tumor. This process was most marked in the region of the cauda, which seemed to account adequately for the weakness of the legs. There was some infiltration in the cervical region, but it hardly seemed enough to explain the severe pains in the arms, neck and head or their sudden development. I think that nerve roots must have been caught in the tumor infiltration at some point that we failed to discover. There was evidence of old thrombophlebitis in the iliac vein.

CASE 32282

PRESENTATION OF CASE

A fifty-year-old chauffeur entered the hospital because of epigastric pain.

The patient was apparently well until a week before admission, when he had an attack of evening "indigestion" accompanied by severe, dull, gnawing, nonradiating epigastric pain ("as if the stomach were twisting"), a feeling of pressure and a great deal of belching. He called his doctor, and was given morphine. The next day the symptoms had ceased. Two nights before entry, he had a similar episode and again received morphine. The night before admission there was a third recurrence of pain, which persisted until the following day despite two injections of morphine. He had no fever, chills, vomiting or nausea. His last bowel movement was one day before entry. His appetite was good until the present illness. There was no previous history of gastric distress, but he had always avoided fried foods and gravy. Six years before entry, the patient had an episode of weakness, at which time an electro-

cardiogram was reported as normal. There was no history of recent weight loss.

Physical examination revealed a drowsy man with constricted pupils who was still suffering from epigastric distress. The pupils responded to light. The tongue was dry and coated with a yellow film. The heart and lungs were normal. The abdomen was somewhat tense but not tender. No masses were felt.

The blood pressure was 130 systolic, 85 diastolic. The temperature was 99.5°F, the pulse 90, and the respirations 20.

Examination of the blood revealed a hemoglobin of 16.1 gm. and a white-cell count of 17,400, with 85 per cent neutrophils. The urine was negative except for a + test for albumin.

A plain film of the abdomen revealed a moderate quantity of gas and fecal material in the colon. In the right midabdomen there was a gas-filled loop of small bowel, which was not dilated. There were calcified lymph nodes just to the right of the lumbar spine. Two ring shadows were seen in the gall-bladder region. When the patient assumed the upright position one of these shadows dropped to the fundus, but the other remained in the region of the cystic duct.

At 2.00 p.m. on the day of admission, the patient was free of pain but still moderately under the influence of morphine. There was minimal residual tenderness over the area of the gall bladder. At 5.00 p.m. there was a recurrence of pain, subjectively located in the upper epigastrium. On palpation the right upper quadrant was much more rigid than the left. Sharp pain was elicited on palpation in the right upper quadrant just lateral to the border of the rectus muscle, and one observer felt a suggestion of a soft mass in that area. Morphine was again administered. By evening the abdominal spasm was limited to this rather sharply defined zone along the right costal margin, where another observer thought that he could feel a mass. The patient felt fairly well, but the temperature had risen to 102°F and the white-cell count to 21,050.

On the second hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CLAUDE E. WELCH. In essence, this is the history of a fifty-year-old man with repeated attacks of severe epigastric pain that occurred within a week. The discussion of the differential diagnosis may be quickly limited to the gall bladder, pancreas, stomach and duodenum. In other words, was this an acute gall-bladder condition, acute pancreatitis or a perforated peptic ulcer?

The history eliminates the least likely diagnosis, perforated peptic ulcer. The patient had attacks of severe pain at intervals, but between them he was apparently free of distress. This is not the history of perforated ulcer. No mention is made

of a plain film of the abdomen taken with the patient in a sitting posture, probably because the surgeon in charge did not consider perforated ulcer a possible diagnosis.

There is also little in the history to support the diagnosis of pancreatitis, which is usually ushered in by an acute attack of pain that is not remittent. Severe pancreatitis is frequently associated with vomiting. In the later stages, the white-cell count becomes high, although the temperature is likely to remain nearly normal. A blood amylase determination would have been of value so far as this diagnosis is concerned, but none is reported in the record.

One therefore returns to the most probable diagnosis — gall-bladder disease. So far as the exact type of disease is concerned, the intense pain, consisting of repeated steady attacks without nausea and without either chills or jaundice, indicates that there was no common-duct involvement and that the obstruction was in the cystic duct. Additional evidence is supplied by the x-ray film, which shows shadows of stone too large to pass through the cystic duct.

The rapidly rising temperature and the rising white-cell count under bed rest in the hospital suggest that a simple acute cholecystitis progressed to empyema. With this deterioration of the patient's condition operation was obviously indicated at an early stage, because of the impending danger of perforation.

There is no unequivocal evidence whether the gall bladder perforated. With a simple empyema of the gall bladder, a mass should have been easily palpable in a patient of normal size, there is nothing in the history to indicate that this patient was obese. Certainly the gall bladder was large when the x-ray film was taken, since one of the stones changed position.

I therefore believe that the gall bladder perforated after the x-ray film was taken and before the operation was performed. My final diagnosis is acute cholecystitis, with gangrene and perforation of the gall bladder and pericholecystic abscess.

DR. MARSHALL K. BARTLETT. When this patient was seen before operation, our line of reasoning was much the same as that of Dr. Welch. The patient had been so heavily medicated before admission that it was difficult to evaluate the exact status of the process, and it was decided to observe him overnight. By the next day it was obvious that the disease was progressing, and operation was deemed advisable. I did not feel a definite mass at any time.

CLINICAL DIAGNOSES

Acute cholecystitis
Cholelithiasis

DR WELCH'S DIAGNOSES

Acute cholecystitis, with gangrene and perforation of gall bladder and pericholecystic abscess
Cholelithiasis

ANATOMICAL DIAGNOSES

Acute and chronic cholecystitis
Cholelithiasis

PATHOLOGICAL DISCUSSION

DR BARTLETT At operation, thirty-six hours after the onset of the attack, there were a few fresh adhesions to the gall bladder, which was tense, edematous and obviously acutely inflamed. It

contained several large stones. The cystic duct was small. Nothing abnormal was felt in the common duct, which was therefore not explored. The cystic duct and artery were isolated and tied. The gall bladder was removed in the usual manner without particular difficulty. The patient made an uneventful recovery, and was discharged on the eleventh day after operation.

DR BENJAMIN CASTLEMAN The gall bladder that we received in the laboratory was edematous and porky and measured 7 mm in thickness. A large patch of fibrinous exudate was present on the serosal surface, and the mucosa was markedly hemorrhagic and necrotic. There was therefore evidence of both acute and chronic inflammation.

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HOSPITALS FACE CRITICAL SITUATION

Most of the hospitals in the Boston area are experiencing great difficulty in getting enough people to care for their patients. This includes graduate nurses, licensed attendants, ward helpers and ward maids.

The salaries of all these groups of people have been advanced to meet the increased cost of living. When all is said and done, the salaries of nurses compare favorably with those paid in government hospitals when it is realized that nurses working in civilian hospitals can choose their place of occupation.

There is no question that there is a shortage of nurses. No one knows just why whether it is

because so many nurses are getting married, whether so many nurses are accepting their privileges under the G I Bill of Rights, whether so many nurses are engaged in private duty, or whether so many nurses are entering service in the hospitals of the Army, Navy, Veterans Administration and Public Health Service. One cannot help wondering whether nurses realize the full seriousness of the situation in relation to the public's health.

The Massachusetts General Hospital had to close 80 of its beds in May, although a few of these were reopened in June. The Massachusetts Eye and Ear Infirmary is facing a serious shortage of nurses and has had to close its children's ward and nursery, emergency children's cases, however, are admitted and cared for in a section of the adult ward.

Hospital trustees, administrators, institutional nurses and employees have done and are doing everything that they can think of to remedy this situation. Little more can be done other than to let everyone, including patients, potential patients, possible employees, physicians, nurses and others, know what the situation is. The matter has now become a community as well as a hospital problem.

LIFE INSURANCE MEDICAL RESEARCH FUND STARTS SECOND YEAR

It is generally agreed that fundamental research in science is useful and deserving of support. It is also well known that such research has become increasingly expensive and that the funds available for that purpose have not kept pace with the growing needs. Because the prospects of sustaining and expanding research in the physical and biologic sciences by private funds are steadily diminishing, new sources for support of activities in these fields have been sought. The many useful results achieved by governmental support of scientific research connected with the war effort have stimulated activity in favor of inaugurating a system whereby the physical and biologic sciences and scientists in these fields could receive appropriate aid from governmental funds. Most scientists, however, suspect that such support implies political dictation and control, as well as an unnecessary amount of red tape. They therefore prefer other sources of funds, if they

can be provided. Those who hold that opinion believe that all possible private sources should be explored and that these agencies should be encouraged to provide the necessary funds, free of all encumbrances.

With respect to research in the medical sciences, its primary and long range purpose, broadly speaking, is to keep the greatest number of people in the best of health for the longest time. That purpose coincides exactly with the objectives of all life-insurance companies. To them the accomplishment of this purpose means increasing returns in terms of dollars and cents. It is therefore not surprising that executives of the majority of the large life-insurance companies in the United States and some in Canada have pooled funds for the support of basic research in medical problems and have entrusted these funds to an organization called the Life Insurance Medical Research Fund. The advisory council of this fund includes a group of medical investigators from different universities, most of whom have had considerable experience with the administration of research funds.

The first annual report of the Life Insurance Medical Research Fund, that for the year 1945, has recently been mailed to the one hundred and forty-eight sponsoring companies in the United States and Canada. During that time \$126,525 was earmarked for grants already approved for eight research projects underway at six medical schools. Because of conditions associated with the termination of the war, only 25 per cent of the annual contributions of the various member companies was called for in 1945, but it is the intention of the fund to call for full contributions, amounting to approximately \$580,000, in 1946. The chairman of the Board of Directors of the Fund states that the program holds much promise of good for both policyholders and the general public. The type of research that is being supported is fundamental in character and concerns, among other things, investigations into the basic causes of rheumatic fever, hypertension and arteriosclerosis. It is fully appreciated that tangible results in such researches must not be looked for too soon, and it is implied that the Fund will continue to support plans of research on a long-term basis.

There are many other private groups that would also benefit by developments along similar lines. Thus, the manufacturers of pharmaceuticals and industrialists in general have long-range interests in this field, and their promotion of fundamental research by the financial support of teachers and investigations in medical sciences could not fail to be a good investment. They should be encouraged to follow the lead of the life-insurance companies.

MASSACHUSETTS MEDICAL SOCIETY

SUBCOMMITTEE ON VETERANS' AFFAIRS, COMMITTEE ON POSTWAR PLANNING

The Subcommittee on Veterans' Affairs, composed of G. Philip Grabfield, chairman, Victor G. Balboni, George P. Denny, Alexander Marble and George F. Wilkins, has been enlarged to include representatives of all the district medical societies. The representatives thus far appointed are as follows:

Barnstable Sheldon L. Hunt, Yarmouth Port
Berkshire Franklin K. Paddock, Pittsfield
Bristol North Leonard W. Hill, Attleboro
Bristol South Merrill F. Gardner, Fairhaven
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Middlesex South John C. McGirr, Belmont
Norfolk Leo R. Desmond, Dorchester
Norfolk South Ensio K. F. Ronka, Wollaston
Plymouth William M. Carr, Whitman
Suffolk Charles H. Bradford, Boston
Worcester Thomas Hunter, Shrewsbury

Any veteran physician with problems or suggestions in relation to veterans' affairs should communicate with his district representative or the chairman.

G. PHILIP GRABFIELD, *Chairman*

MISCELLANY

PUBLIC-HEALTH CONFERENCE IN CHINA

News has been received from Lieutenant Colonel Merrill Moore, M.C., A.U.S., to the effect that he took an active part in the organization of the first public-health conference to be held in China during the past ten years. The conference was sponsored by Major General Robert B. McClure, commanding general of the Nanking Headquarters Command, United States Army Forces, and by General Ho Yin-Ching, supreme commander of the Chinese Army, and was held on Saturday, April 20, in the Assembly Hall of the Supreme Headquarters of the Chinese Army at Nanking. The program comprised sixteen addresses, the majority in Chinese, having to do with various aspects of preventive medicine and hygiene.

BOOKS RECEIVED

The receipt of the following book is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

What to Do about Vitamins By Roger J. Williams, Ph.D., director of the Biochemical Institute, University of Texas 8°, cloth, 56 pp. Norman, Oklahoma: University of Oklahoma Press, 1945. \$1.00

This popular manual discusses the necessity of vitamins and minerals in the diet and how they may be secured in adequate amounts. The text is illustrated with tables, graphs and charts for easy reference. Appended to the text is an interesting table of the vitamin content of the common foods, both vegetable and animal.

Total War and the Human Mind: A psychologist's experiences in occupied Holland By A. M. Meerloo, M.D., F.R.S.M. 8°, cloth, 78 pp. New York: International Universities Press, Incorporated, 1945. \$1.75

In this book Dr. Meerloo has drawn on his experiences of two years in occupied Holland and discusses such themes as mass reaction to German occupation, Hitler's psychological weapons, the psychology of radio propaganda and how the body is affected by fear.

Pharmaceutical Calculations By Willis T. Bradley, A.M., and Carroll B. Gustafson, Ph.C., A.M. 8°, cloth, 283 pp. Philadelphia: Lea and Febiger, 1945. \$2.75

This manual is based on the *Pharmaceutical Arithmetic* of Professor Theodore J. Bradley but is substantially a new work, since it includes theoretical discussions and explanations preceding examples and practice deliberately excluded from the original work.

Much new material has been added, including a simplified equation for converting centigrade and Fahrenheit scales, a new approach to ratio and percentage and dilution problems consistent with the *Pharmacopoeia* and an original treatment of isotonic problems.

It includes careful definition of terms and is intensely practical in its application. Appendices contain related matter on problems in general chemistry, weights and volumes of gases, proof strength, emulsions, solubility ratios and tables of epitonic equivalents, dilution, weight and volume of water and atomic weights.

This small volume should prove of value not only to students and teachers of pharmacy but also to pharmacists, chemists, physicians, nurses and all others confronted with the problems of arithmetical problems in pharmacy. It is recommended for reference purposes to medical and allied libraries.

Lights Out By Baynard Kendrick. 8°, cloth, 240 pp. New York: William Morrow and Company, 1945. \$2.50

This is the story of a blinded soldier and his conditioning in Army hospitals for a normal everyday life.

The Male Hormone By Paul de Kruif. 8°, cloth, 243 pp. New York: Harcourt, Brace and Company, 1945. \$2.50

DeKruif, in another of his popular books on medical subjects, narrates the story of the long struggle to isolate the male hormone until its discovery by the chemists, Ruzicka and Bubenandt, in 1935, who later were awarded the Nobel prize for their work. The author then relates in plain language the use of testosterone in revitalizing men suffering from poor health due to sexual insufficiency.

Your Hair and Its Care By Oscar I. Levin, M.D., and Howard T. Behrman, M.D. 12°, cloth, 184 pp. New York: Emerson Books, Incorporated, 1945. \$2.00

The authors are dermatologists who have written in plain language an up-to-date popular manual on the human hair. They tell what to do to save and beautify the hair and to stimulate healthier growth and discuss such conditions as baldness of various types, dandruff, infections of the scalp, abnormal types of hair and the effects of occupations on the hair.

Moderne Esstherapie By Rudolf Stodtmeister and Peter Büchmann. With introductory remarks by Professor Dr. R. Siebeck, of Heidelberg, and Professor Dr. L. Heilmeyer, of Jena. 8°, cloth, 120 pp. Ann Arbor: J. W. Edwards, Incorporated, 1944. \$3.75. Published and distributed in the Public Interest by Authority of the Alien Property Custodian under License No. A-492.

This monograph in German has been considered of sufficient importance to be reproduced by lithoprinting from the original Stuttgart edition of 1943. This fact alone speaks well for the importance of the work. About half the text discusses the use of iron in the treatment of the anemias, including the pernicious and aplastic types. The first two chapters have to do with the role of iron in the human organism and iron resorption. These are followed by a brief consideration of the general indication of iron in treatment and then by a section on the clinical use of iron in the anemias. The last short chapter is miscellaneous in character, discussing such topics as blood transfusion and iron therapy, iron and arsenic, iron preparations, length of treatment, intravenous use and liver treatment. The text is compact and in simple German. This monograph should be in all medical libraries and on the shelves of all physicians specializing in blood diseases.

NOTICES

ANNOUNCEMENTS

Dr. R. H. Aldrich announces the removal of his office to 422 Beacon Street, Boston.

Dr. Nathaniel Bennett, having returned from military service, announces the opening of an office at 646 Summer Avenue, Springfield.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 18

FRIDAY, JULY 19

*10:00 a.m.-12:00 p.m. Medical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY, JULY 23

*12:00 p.m.-1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater, Dowling Building, Boston City Hospital.

12:15-1:15 p.m. Clinicorontgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JULY 24

*10:30-11:30 a.m. Medical Clinic. Isolation Building. Amphitheater, Children's Hospital.

*12:00 p.m. Clinicopathological Conference (Children's Hospital). Amphitheater, Peter Bent Brigham Hospital.

*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

*Open to the medical profession.

MARCH 15-SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240. Issue of February 14.

SEPTEMBER 4-7. American Congress of Physical Medicine. Page 616. Issue of May 2.

SEPTEMBER 30-OCTOBER 3. Industrial Health Congress. Page 878. Issue of June 27.

OCTOBER 6-12. Interamerican Congress of Cardiology. Page xix. Issue of June 6.

OCTOBER 7-18. New York Academy of Medicine. Page 544. Issue of April 18.

FEBRUARY 7. American Board of Obstetrics and Gynecology. Page 34. Issue of July 4.

DISTRICT MEDICAL SOCIETY

PLYMOUTH

OCTOBER. Jordan Hospital, Plymouth.

NOVEMBER. Plymouth County Hospital, South Hanson.

JANUARY. Brockton Hospital, Brockton.

FEBRUARY. Moore Hospital, Brockton.

MARCH. Goddard Hospital, Brockton.

APRIL. State Farm, Bridgewater.

MAY. Lakeville Sanatorium, Lakeville.

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Number 3

THE SURGERY OF THE INNOMINATE ARTERY*

GUSTAF E. LINDSKOG, M.D.†

NEW HAVEN, CONNECTICUT

THE first recorded operation on the innominate artery was performed by Valentine Mott of New York on May 11, 1818. Ligation of this vessel in an attempt to cure a traumatic subclavian aneurysm was followed by wound sepsis, secondary hemorrhage and death. Such was the fate of all subsequent surgical attempts in the preaseptic era until the twentieth recorded case, in which a successful ligation for subclavian aneurysm was performed on May 15, 1864, by Andrew Smyth,¹ of New Orleans. This patient was younger, and fate was kinder. Recovery ensued after a terrifying series of hemorrhages, for the treatment of which metallic shot was repeatedly introduced into the suppurating wound. The eventual result was satisfactory, with arrest of symptoms until a recurrence and reoperation caused death eleven years later. Coppinger,² of Dublin, was the first European surgeon successfully to accomplish this formidable ligation. His operation was performed in 1893.

With the advent of antiseptic and finally aseptic technics and with the development of suitable anesthesia procedures, cases accumulated and relatively greater success was enjoyed. In 1905, Sheen³ was able to collect 36 cases, including one of his own, which was the eighth successful ligation. In 1915, Thompson's⁴ review added 16 cases. The latest complete survey of the literature was made by Greenough⁵ in 1929. His report is characterized by accuracy and completeness. It comprises 91 cases and includes ligations, simple sutures, excisions and attempted ligations, besides reporting one personal success. In this series the operative mortality rate was 56 per cent, but in the most recent 25 cases it was only 16 per cent. I have re-examined the available literature and have collected 18 new cases, all of which have appeared since Greenough's summary.

INDICATIONS FOR OPERATION

Ligation of the innominate artery has been performed for four indications: recent wounds of this vessel and its two major branches, 11 cases, traumatic

aneurysm of the innominate, subclavian and carotid arteries, 20 cases, spontaneous—usually syphilitic—aneurysm of these vessels, 75 cases, and control of remote bleeding, 1 case. The indications and results are listed in Table 1. A certain latitude must be permitted in the interpretation of many of the operative reports. Some obscurity in description is comprehensible when one considers the inadequacies of anesthesia, lighting and exposure that hampered the earlier cases. Doubtless some fatal cases have never been reported.

TABLE 1. *Indications for and Results of Ligation of the Innominate Artery*

	No. of Cases	RECOVERIES	
		NO.	PER- CENTAGE
Recent wounds			
Innominate artery	4	2	
Subclavian artery	3	0	
Carotid artery	4	1	
Total	11	3	27
Traumatic aneurysm			
Innominate artery	5	4	
Subclavian artery	12	8	
Carotid artery	3	3	
Total	20	15	75
Spontaneous aneurysm			
Innominate artery	30	15	
Subclavian artery	43	15	
Carotid artery	2	1	
Total	75	31	41
Control of remote hemorrhage	1	0	0
Grand totals	107	49	
Percentage			46

in the literature, but probably few successful cases have so failed, so that the statistical results must be weighted on the favorable side.

There can be no question of the propriety of and necessity for operation in traumatic lesions of the innominate artery and its bifurcation. The situation is urgent, and many of these patients do not survive the immediate injury, which is usually due to a gunshot, shrapnel or stab wound. A most interesting case of transverse rupture of the innominate artery with an intact chest has been reported.⁶ This patient died without benefit of surgery, and the case is not included in the present series.

*Presented at the annual meeting of the New England Surgical Society, Boston, February 6, 1946.

†Associate professor of surgery, Yale University School of Medicine.

BOOKS RECEIVED

The receipt of the following book is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

What to Do about Vitamins By Roger J. Williams, Ph.D., director of the Biochemical Institute, University of Texas, 8°, cloth, 56 pp. Norman, Oklahoma: University of Oklahoma Press, 1945. \$1.00.

This popular manual discusses the necessity of vitamins and minerals in the diet and how they may be secured in adequate amounts. The text is illustrated with tables, graphs and charts for easy reference. Appended to the text is an interesting table of the vitamin content of the common foods, both vegetable and animal.

Total War and the Human Mind: A psychologist's experiences in occupied Holland By A. M. Meerloo, M.D., F.R.S.M. 8°, cloth, 78 pp. New York: International Universities Press, Incorporated, 1945. \$1.75.

In this book Dr. Meerloo has drawn on his experiences of two years in occupied Holland and discusses such themes as mass reaction to German occupation, Hitler's psychological weapons, the psychology of radio propaganda and how the body is affected by fear.

Pharmaceutical Calculations By Willis T. Bradley, A.M., and Carroll B. Gustafson, Ph.C., A.M. 8°, cloth, 283 pp. Philadelphia: Lea and Febiger, 1945. \$2.75.

This manual is based on the *Pharmaceutical Arithmetic* of Professor Theodore J. Bradley but is substantially a new work, since it includes theoretical discussions and explanations preceding examples and practice deliberately excluded from the original work.

Much new material has been added, including a simplified equation for converting centigrade and Fahrenheit scales, a new approach to ratio and percentage and dilution problems consistent with the *Pharmacopoeia* and an original treatment of isotonic problems.

It includes careful definition of terms and is intensely practical in its application. Appendices contain related matter on problems in general chemistry, weights and volumes of gases, proof strength, emulsions, solubility ratios and tables of epitonic equivalents, dilution, weight and volume of water and atomic weights.

This small volume should prove of value not only to students and teachers of pharmacy but also to pharmacists, chemists, physicians, nurses and all others confronted with the problems of arithmetical problems in pharmacy. It is recommended for reference purposes to medical and allied libraries.

Lights Out By Baynard Kendrick. 8°, cloth, 240 pp. New York: William Morrow and Company, 1945. \$2.50.

This is the story of a blinded soldier and his conditioning in Army hospitals for a normal everyday life.

The Male Hormone By Paul de Kruif. 8°, cloth, 243 pp. New York: Harcourt, Brace and Company, 1945. \$2.50.

DeKruif, in another of his popular books on medical subjects, narrates the story of the long struggle to isolate the male hormone until its discovery by the chemists, Ruzicka and Butenandt, in 1935, who later were awarded the Nobel prize for their work. The author then relates in plain language the use of testosterone in revitalizing men suffering from poor health due to sexual insufficiency.

Your Hair and Its Care By Oscar L. Levin, M.D., and Howard T. Behrman, M.D. 12°, cloth, 184 pp. New York: Emerson Books, Incorporated, 1945. \$2.00.

The authors are dermatologists who have written in plain language an up-to-date popular manual on the human hair. They tell what to do to save and beautify the hair and to stimulate healthier growth and discuss such conditions as baldness of various types, dandruff, infections of the scalp, abnormal types of hair and the effects of occupations on the hair.

Moderne Eisen Therapie By Rudolf Stodtmeister and Peter Büchmann. With introductory remarks by Professor Dr. R. Sicbeck, of Heidelberg, and Professor Dr. L. Heilmeyer, of Jena. 8°, cloth, 120 pp. Ann Arbor: J. W. Edwards, Incorporated, 1944. \$3.75. Published and distributed in the Public Interest by Authority of the Alien Property Custodian under License No. A-492.

This monograph in German has been considered of sufficient importance to be reproduced by lithoprinting from the original Stuttgart edition of 1943. This fact alone speaks well for the importance of the work. About half the text discusses the use of iron in the treatment of the anemias, including the pernicious and aplastic types. The first two chapters have to do with the role of iron in the human organism and iron resorption. These are followed by a brief consideration of the general indication of iron in treatment and then by a section on the clinical use of iron in the anemias. The last short chapter is miscellaneous in character, discussing such topics as blood transfusion and iron therapy, iron and arsenic, iron preparations, length of treatment, intravenous use and liver treatment. The text is compact and in simple German. This monograph should be in all medical libraries and on the shelves of all physicians specializing in blood diseases.

NOTICES

ANNOUNCEMENTS

Dr. R. H. Aldrich announces the removal of his office to 422 Beacon Street, Boston.

Dr. Nathaniel Bennett, having returned from military service, announces the opening of an office at 646 Summer Avenue, Springfield.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 18

FRIDAY JULY 19

*10:00 a.m.-12:00 p.m. Medical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY JULY 23

*12:00 p.m.-1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater Dowling Building, Boston City Hospital.

12:15-1:15 p.m. Clinicorontgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JULY 24

*10:30-11:30 a.m. Medical Clinic. Isolation Building, Amphitheater Children's Hospital.

*12:00 p.m. Clinleopathological Conference (Children's Hospital). Amphitheater Peter Bent Brigham Hospital.

*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater Children's Hospital.

*Open to the medical profession.

MARCH 15-SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240. Issue of February 14.

SEPTEMBER 4-7. American Congress of Physical Medicine. Page 616. Issue of May 2.

SEPTEMBER 30-OCTOBER 3. Industrial Health Congress. Page 878. Issue of June 27.

OCTOBER 6-12. Interamerican Congress of Cardiology. Page xix. Issue of June 6.

OCTOBER 7-18. New York Academy of Medicine. Page 544. Issue of April 18.

FEBRUARY 7. American Board of Obstetrics and Gynecology. Page 34. Issue of July 4.

DISTRICT MEDICAL SOCIETY

PLYMOUTH

OCTOBER. Jordan Hospital, Plymouth.

NOVEMBER. Plymouth County Hospital, South Hanson.

JANUARY. Brockton Hospital, Brockton.

FEBRUARY. Moore Hospital, Brockton.

MARCH. Goddard Hospital, Brockton.

APRIL. State Farm, Bridgewater.

MAY. Lakeville Sanatorium, Lakeville.

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THE SURGERY OF THE INNOMINATE ARTERY*

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NEW HAVEN, CONNECTICUT

THE first recorded operation on the innominate artery was performed by Valentine Mott of New York on May 11, 1818. Ligation of this vessel in an attempt to cure a traumatic subclavian aneurysm was followed by wound sepsis, secondary hemorrhage and death. Such was the fate of all subsequent surgical attempts in the preaseptic era until the twentieth recorded case, in which a successful ligation for subclavian aneurysm was performed on May 15, 1864, by Andrew Smyth,¹ of New Orleans. This patient was younger, and fate was kinder. Recovery ensued after a terrifying series of hemorrhages, for the treatment of which metallic shot was repeatedly introduced into the suppurating wound. The eventual result was satisfactory, with arrest of symptoms until a recurrence and reoperation caused death eleven years later. Coppinger,² of Dublin, was the first European surgeon successfully to accomplish this formidable ligation. His operation was performed in 1893.

With the advent of antiseptic and finally aseptic technics and with the development of suitable anesthesia procedures, cases accumulated and relatively greater success was enjoyed. In 1905, Sheen³ was able to collect 36 cases, including one of his own, which was the eighth successful ligation. In 1915, Thompson's⁴ review added 16 cases. The latest complete survey of the literature was made by Greenough⁵ in 1929. His report is characterized by accuracy and completeness. It comprises 91 cases and includes ligations, simple sutures, excisions and attempted ligations, besides reporting one personal success. In this series the operative mortality rate was 56 per cent, but in the most recent 25 cases it was only 16 per cent. I have re-examined the available literature and have collected 18 new cases, all of which have appeared since Greenough's summary.

INDICATIONS FOR OPERATION

Ligation of the innominate artery has been performed for four indications: recent wounds of this vessel and its two major branches, 11 cases, trau-

matic aneurysm of the innominate, subclavian and carotid arteries, 20 cases, spontaneous—usually syphilitic—aneurysm of these vessels, 75 cases, and control of remote bleeding, 1 case. The indications and results are listed in Table 1. A certain latitude must be permitted in the interpretation of many of the operative reports. Some obscurity in description is comprehensible when one considers the inadequacies of anesthesia, lighting and exposure that hampered the earlier cases. Doubtless some fatal cases have never been reported.

TABLE 1 *Indications for and Results of Ligation of the Innominate Artery*

	No of Cases	RECOVERIES	
		NO	PER- CENTAGE
Recent wounds			
Innominate artery	4	2	
Subclavian artery	3	0	
Carotid artery	4	1	
Total	11	3	27
Traumatic aneurysm			
Innominate artery	5	4	
Subclavian artery	12	8	
Carotid artery	3	3	
Total	20	15	75
Spontaneous aneurysm			
Innominate artery	30	15	
Subclavian artery	43	15	
Carotid artery	2	1	
Total	75	31	41
Control of remote hemorrhage	1	0	0
Grand totals	107	49	
Percentage			46

in the literature, but probably few successful cases have so failed, so that the statistical results must be weighted on the favorable side.

There can be no question of the propriety of and necessity for operation in traumatic lesions of the innominate artery and its bifurcation. The situation is urgent, and many of these patients do not survive the immediate injury, which is usually due to a gunshot, shrapnel or stab wound. A most interesting case of transverse rupture of the innominate artery with an intact chest has been reported.⁶ This patient died without benefit of surgery, and the case is not included in the present series.

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The problem of syphilitic or nonspecific aneurysm — hereafter called "spontaneous aneurysm" — calls for more detailed consideration and evaluation of data. Practically all these patients have had diffuse arterial and complicating visceral disease. They have an average age (forty-seven years) older than that (twenty-eight years), in the traumatic cases, and the danger of concomitant visceral complications is consequently greater. The incidence of therapeutic failure, especially after simple ligation, is higher in these cases than in the traumatic cases. Yet the life of a patient afflicted with such an aneurysm is usually a miserable one because of pressure symptoms, which include severe pain, dysphagia, hoarseness and dyspnea, and there is always the ominous threat of rupture into the pleural cavity or trachea or through the skin as a terminal event.

A few reported cases with small aneurysms in the third subclavian area, because of their small size and position, the presence of brachial pain and the absence of clinical syphilis, are reminiscent of aneurysm due to cervical rib. If so, they hardly constitute a proper indication for the operation as performed, since this type of case does not have a tendency to progression and is satisfactorily handled by local surgery.⁷

METHODS OF TREATMENT

The ideal treatment of an aneurysm, whether traumatic or spontaneous, is either a Matas end-aneurysmorrhaphy or proximodistal ligation and excision of the sac.⁸ In the case of the innominate artery, the Matas operation does not lend itself to practical application, and there is no record of its deliberate use. Complete isolation and excision of the sac have been accomplished in only 3 cases, in all of which they were successful. Resort to the simpler procedure of ligation in continuity has been the rule, owing to technical difficulties or to the patient's condition. Proximal ligation of the innominate artery, with ligation of the carotid and subclavian arteries distal to the aneurysm — the so-called "triple operation" — has been performed more frequently than has radical excision, and the results have been better than those of proximal ligation alone.⁴ Better surgical technic and more favorable operative conditions may have contributed to this difference.

In the case to be reported, a preliminary ligation of the common carotid artery was performed to test the cerebral circulation, promote the development of collaterals and prevent subsequent cerebral embolism or propagating thrombosis following direct operative trauma to the aneurysmal sac. Cerebral complications (Table 2) are reported to have caused postoperative death in 9 cases, and temporary disability in a few others. The average age in the fatal cerebral cases was 40.0 years, as compared with 42.5 years for the entire series. These

facts suggest that the inherent vascular pattern is of more importance than the age factor.

Not a single case has been reported in which gangrene of the upper extremity followed ligation of the innominate artery, a fact that emphasizes the abundant collateral vascular pathways in the shoulder girdle and axilla (intercostal-subscapular). The

TABLE 2 Cause of Death

CAUSE OF DEATH	No. of Cases
Sepsis	6
Sepsis, with later hemorrhage	14
Late hemorrhage	11
Operative hemorrhage	3
Other operative accidents	11
Cerebral complications	9
Renal complications	1
Bronchopneumonia	2
Unstated	1
Total	58

occurrence of late ischemic pain, paresthesia and muscular weakness in the arm, however, has occasionally been noted and quite generally disregarded from the therapeutic standpoint. No mention has been made in recent years of the postoperative use of sympathetic block or dorsal sympathectomy. Although aneurysm of the innominate artery frequently produces Horner's syndrome on the right, there is recorded evidence in some cases that a sympathetic release with vasodilatation occurs in the vessels of the right upper extremity within twelve to twenty-four hours after operation. This phenomenon was noted in my patient, who has complained of no ischemic symptoms in the arm since operation.

In view of the technical difficulties connected with exposure of the innominate artery and the high mortality in the earlier cases, various indirect or simpler therapeutic approaches for aneurysm of this artery have been devised and tried. One is the application of the wiring technic, which has been associated with uncertain results and with the complications pertaining to this method in other vessels.⁹ A second is the technic of Brasdor-Guinar — namely, ligation of the subclavian and carotid arteries distal to the aneurysmal sac. With the use of this method, long-term cures of five to twenty-one years have been reported by Baldwin,¹⁰ Schwyzer,¹¹ DaCosta (cited by Rundle¹²) and others. This procedure has been condemned by some authors, but analysis of the reports suggests that there is some prospect of relief or cure when a more radical approach is contraindicated by diffuse aortic disease, the patient's age or his general condition.

Finally, innominate aneurysm has been treated by the creation of an arteriovenous fistula between the common carotid artery and the jugular vein, with an end-to-end technic, as first suggested by Babcock. McCarthy¹³ has reported 8 such cases,

TABLE 3 *Successful Cases of Ligation of Innominate Artery for Aneurysm*

SURGEON	YEAR REPORTED	YEAR OF OPERATION	SEX	AGE	PATHOLOGIC LESION	TYPE OF INCISION	ARTERY OR ARTERIES LIGATED	REMARKS	LAST REPORT
Burrell (Greenough ⁵)	1895	1895	M	4	Spontaneous aneurysm (subclavian and innominate)	Resection of portion of sternum	Innominate	Discharged from hospital on 73rd day cardiac death on 104th day	
Cunéo (Greenough ⁵)	1911	1905	F	49	Spontaneous aneurysm (innominate and aortic)	Supraclavicular	Innominate		Well in Dec., 1910
Sargent (Greenough ⁵)	1911	1909	F	67	Spontaneous aneurysm (bifurcation)	Resection of manubrium	Innominate and carotid	Transient hemiplegia on 10th day	Died in 1911 of nephritis and pneumonia sac obliterated at autopsy
Kimura (Greenough ⁵)	1913	1908	M	46	Spontaneous aneurysm (bifurcation)		Innominate carotid and subclavian	Cured	Well in Apr., 1910
Ballance (Greenough ⁵)	1918	1918	F	60	Spontaneous aneurysm (innominate) (syphilitic)		Innominate		Died on June 5 1921 sac occluded at autopsy
Halsed (Greenough ⁵)	1926	1907	M	61	Spontaneous aneurysm (bifurcation)		Innominate artery (later band to carotid)	Pulsation ceased	Death from pneumonia on Jan 1 1908
Lessner (Greenough ⁵)	1928	1914	M	—	Traumatic aneurysm (innominate)	Supraclavicular	Innominate	Radial pulse returned before discharge	Well
Flint (Greenough ⁵)	1928	1927	M	7	Traumatic aneurysm (bifurcation)	Excision of of manubrium	Innominate and subclavian	Aneurysmal sac packed	Well 5 mo later poor vision of right eye husky voice.
Greenough (Greenough ⁵)	1929	1924	F	48	Spontaneous aneurysm (bifurcation)	Sternoclavicular disarticulation	Innominate carotid and subclavian	Wound sepsis	Well in Apr 1925
Miller Dolbey and Ballance ¹⁸	1934	1925	M	74	Spontaneous aneurysm (innominate) (positive serologic reaction)	Resection of clavicle and manubrium	Innominate	Subsequent ligation of carotid and subclavian arteries in 1925	Recurrence with rupture and death in Oct 1933
Scouttar ¹⁹	1934	1933	F	62	Spontaneous aneurysm (innominate) (negative serologic reaction)	Supraclavicular	Innominate and subclavian	Traumatic hemiparesis at 7 mo	Well
Rock (Rundle ¹²)	1937	1936	F	49	Spontaneous aneurysm (innominate) (positive serologic reaction)		Innominate carotid and subclavian		Living (with paresis) 3 yr later
Edwards (Rundle ¹²)	1937	1935	F	64	Spontaneous aneurysm (innominate)		Innominate	Recurrence (see next case)	
Rock (Rundle ¹²)	1937	1936	F	64	Recurrence (see previous case)	Sternotomy	Innominate carotid and subclavian (excision of sac)		Well in 1937
Matas ⁸	1940	Not stated	Not stated	Not stated	Spontaneous aneurysm (innominate)		Innominate band		Result not stated
		Not stated	Not stated	Not stated	Spontaneous aneurysm (innominate)		Innominate band		Result not stated
Meade ²⁰	1941	1936	F	65	Spontaneous aneurysm (innominate and subclavian) (negative serologic reaction)	Supraclavicular	Carotid and subclavian (fascial strips)	Pulsation persisted	Improved
Elkin ¹⁵	1945	1945	M	25	Traumatic arteriovenous aneurysm (innominate)	Resection of clavicle and manubrium	Innominate (also right innominate vein)		Well in May 1945
Lindskog	1946	1945	M	27	Traumatic aneurysm (innominate)	Section of clavicle and manubrium	Innominate	Preliminary carotid ligation	Well in 1946

all with positive serologic reactions at the time of operation. There were 2 operative deaths, one apparently due to anesthesia and the other to embolism, and 2 later deaths, one at five weeks from myocardial failure and the other at four weeks from rupture of the aneurysm. Four patients survived, 1 for more than four years, and 2 of them were able to resume work. These results and the generally recognized deleterious effect of a large arteriovenous fistula seem to make some other procedure a wiser choice.

THE SURGICAL APPROACH TO THE INNOMINATE ARTERY

The earliest operations on the innominate artery were carried out through a cervical or supra-clavicular muscle-cutting incision, of which the pro-

section or resection. A median section of the manubrium carried through to the second interspace, with section of the right clavicle in its medial third, gave an adequate exposure and a good functional result in my case. Elkin¹⁵ has described the resection type of approach in detail.

In 107 reported cases of ligation or suture of the innominate artery, the immediate operative mortality was 54 per cent. Two of Greenough's cases are not included, since they represent incomplete attempts with survival. Since 1900 there have been reports of 61 cases, with 19 postoperative deaths, a mortality of 31 per cent. The principal causes of death are summarized in Table 2. It is evident that complications of wound sepsis, including mediastinitis, empyema, pneumonia and hemorrhage, have caused the largest group of fatalities. Acci-

TABLE 4 Other Cases of Ligation of Innominate Artery for Aneurysm Since 1929

SURGEON	DATE OF REPORT	DATE OF OPERATION	SEX	AGE	PATHOLOGIC LESION	TYPE OF INCISION	ARTERY OR ARTERIES LIGATED	REMARKS	RESULT
Chapman ²¹	1929	1928	M	33	Traumatic aneurysm (subclavian)	Section of clavicle	Innominate and carotid	Rupture of sac during excision, wound sepsis, empyema	In good condition 6 mo later
Lexer ¹⁶	1934	1934	M	24	Traumatic arteriovenous aneurysm (innominate)	Bilateral section of clavicle and resection of manubrium	Innominate (transvenous plication) also, ligated innominate vein	Streptococcal sepsis, pleurisy	Death on 17th day
Turner (Rundle) ¹²	1937	1934	M	67	Spontaneous aneurysm (innominate) (positive reaction serologic)		Innominate (attempted)	Previous ligation of subclavian and carotid arteries in Jan., 1933	Death from hemorrhage on 4th day
Matas ⁹	1940	Not stated	Not stated	Not stated	Spontaneous aneurysm (innominate)		Innominate (metal band)	Hemorrhage and pulmonary complications	Death on 6th day
		Not stated	Not stated	Not stated	Traumatic aneurysm (carotid)		Innominate	Cerebral complications	Postoperative death with hemorrhage
Brock ²²	1940	1939	M	66	Spontaneous aneurysm (innominate and aortic) (syphilitic)		Innominate	Wound sepsis and hemorrhage	Death 5 wk. later
Wheeler ²³	1942	1932	M	35	Traumatic aneurysm (subclavian)	Section of clavicle and sternum	Innominate carotid and subclavian	No pulsation after 4 mo	Sudden death in Sept., 1940 cause unknown
Langley ²⁴	1943	1943	M	23	Shrapnel wound (innominate)	Section of clavicle	Innominate carotid and subclavian	Shock, hemiplegia and pulmonary edema	Death in 16 hr

totype is Mott's. This has been adequate in some cases, particularly when the lesion was distal to the innominate artery and when the latter was at a high level.

The first mention of clavicular resection is in Cooper's case report cited by Greenough.⁵ In 1895, Burrell¹⁴ of Philadelphia first resected a portion of the sternum in this connection, and his patient survived ligation. It seems clear that adequate and safe exposure for surgery of the innominate artery demands some type of clavicular and manubrial

dissection of technic follow in importance, after which come cerebral complications. Age appeared to have little or no relation to prognosis in this series, since the average stated age in the fatal cases was 42 years, whereas it was 43 years in the surviving cases.

ARTERIOVENOUS FISTULA

There are 3 recorded cases in which an arteriovenous fistula was treated by surgery of the innominate artery. Holman⁸ in 1927 reported a case in which a subclavian arteriovenous aneurysm was

ruptured during dissection, necessitating ligation of the proximal innominate artery as an emergency procedure. The patient recovered and was apparently cured. Lexer's¹⁶ patient had an aneurysmal varix of the innominate artery and left innominate vein following a stab wound. A transvenous arterial suture was performed, but death occurred from streptococcal sepsis. Elkin¹⁵ in 1945 reported a case of fistula between the artery and both innominate veins. This fistula, which also followed a stab wound, was treated by ligation and section of the right innominate vein and double ligation of the artery. The patient made a good recovery.

No discussion of surgical procedures involving the innominate artery is complete without mention of the recent work of Blalock and Taussig.¹⁷ In an attempt to increase the volume of pulmonary circulation in cases of congenital pulmonic atresia or stenosis, the normal innominate artery has been divided and the proximal end anastomosed to one of the pulmonary arteries.

CASE REPORT

A 27-year-old man was admitted by air transport to a United States naval hospital on August 30, 1945, with a chief complaint of severe pain in the right chest and swelling in the right side of the neck. On May 24, he had been injured by shrapnel from enemy air bombardment on Ie Shima, sustaining multiple small wounds of the right forearm, left foot and right shoulder and a small, sucking wound of the right supraclavicular region. He was rendered immediately unconscious but regained consciousness on the second day without major surgical intervention. He was aphonic for 10 days, had difficulty in vision for 1 week and noted a prominent mass in the lower right side of the neck. The voice improved gradually. On June 12, a bruit was discovered in the right supraclavicular region, and a roentgenogram of the chest showed an enlarged superior mediastinal shadow on the right side. On July 13, the patient had sudden, excruciating pain in the right side of the chest and neck, increased swelling of the mass and painful swallowing, even of liquids. This episode left a sequel of recurring severe pain in the sub-sternal region and right shoulder and frequent headaches. The pain required a routine administration of morphine.

Physical examination on admission revealed a chronically ill man. The face and lips appeared slightly pale and cyanotic. The right palpebral fissure was narrowed, and the pupil was small. The voice was high pitched, and there was a paralysis of the right vocal cord. The trachea was deviated to the left because of a large visible and palpable mass deep in the supraclavicular and jugular region. The mass pulsated during systole, but there was no definite thrill or bruit. The carotid and radial pulses were palpable bilaterally and about equal in volume. Simultaneous brachial blood pressures were 116/80 on the right and 114/75 on the left. There were small, healed wounds of the right wrist, right anterior deltoid region, right supraclavicular region and left foot. The direct measurements of venous pressures in the antecubital fossae were right, 190 mm. of saline solution and left, 185 mm., with free respiratory excursions.

Laboratory studies revealed a negative Kahn reaction and a normal urine. The hemoglobin was 14.5 gm. per 100 cc., and the white-cell count 9000.

A roentgenogram of the chest demonstrated a diffuse widening of the superior mediastinal shadow, continuous with the ascending aorta. The trachea was narrowed and displaced toward the left. There was an irregular, radio-opaque foreign body in the left chest just above the aortic arch. A diagnosis of traumatic aneurysm of the innominate artery from a shrapnel wound was made.

Complete bed rest was enforced. Digital compression of the right carotid artery above the mass in the neck for 5 minutes hourly was begun on September 4. On September 19, ligation of the right common carotid artery was carried out just

proximal to its bifurcation, under local anesthesia. This procedure resulted in a 3-day period of nausea and vomiting but no paresis of the left extremities and no change in blood pressure. On October 3, under intratracheal cyclopropane anesthesia, a trans-sternal anterior mediastinotomy was performed, with ligation of the proximal innominate artery. An incision was made with a horizontal arm just above and parallel to the median half of the clavicle, a vertical component over the midline sternum and a shorter horizontal component over the right 3rd costal cartilage. The proximal portion of the 2nd right costal cartilage was excised, the sternal body was retracted slightly at this level, and the manubrium was split vertically with a Gigli saw introduced from above. The right clavicle was divided. By prolonged and difficult dissection in the densely scarred mediastinal connective tissue, the right and left innominate veins and superior vena cava were mobilized. Both had been displaced and flattened by a large fusiform dilatation of the innominate artery. By dissecting below and above the left innominate vein, a short but relatively normal proximal portion of this artery was freed and a braided linen umbilical tape was passed about it. Temporary occlusion of the vessel resulted in an obliteration of the right radial pulse. The ligature was secured, and a braided-silk ligature was placed above it. The chest was closed with wire sutures to the clavicle and sternum. A rubber-slip drain was left in the wound for 48 hours because of troublesome oozing, which had been particularly noticeable during the initial stages of the chest-wall incision.

Penicillin was given immediately after operation and continued during the 1st week. Early convalescence was complicated by restlessness, euphoria, disorientation, a rapid pulse and elevation of the systolic blood pressure to 150 or 170. The right arm and hand were cool and pale until the morning of the 2nd postoperative day, when warmth and superficial vasodilatation were observed. On the 3rd day, a loud, continuous murmur was heard in the pulmonic area and over the great vessels of the left neck, but only faintly on the right side. This gradually subsided and disappeared. The wound healed well.

A written communication from the patient in December, 1945, indicated continuing improvement, with complete relief of pain and sensations of pressure. There was still some non-pulsating fullness in the clavicular region.

SUMMARY

The literature on the subject of surgery of the innominate artery is reviewed, and the indications for and the technic and results of operation are discussed.

Eighteen cases have been added since a review by Greenough in 1929, and a total of 107 cases of ligation, excision or suture of the innominate artery, with an operative mortality of 54 per cent, are recorded.

Since 1900 there have been 61 cases, with a mortality of 31 per cent.

Nineteen cases of survival after surgery for innominate aneurysm, including the present case, are tabulated. A report of this case is presented.

789 Howard Avenue

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AN OUTLINE FOR THE TREATMENT OF SEVERE BURNS*

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AT THE end of a three-year study of burns at the Boston City Hospital, the following outline of directions for their care has been prepared for the guidance of the hospital staff. This outline has been available at the hospital since July 1, 1945.

DUTIES OF THE ACCIDENT-FLOOR PERSONNEL

Take temperature, pulse, blood pressure and respiration. Remove clothing and place patient on sterile sheet. Cover with sterile sheet.

Inspect area of burn and plot on a Boston City Hospital Burn Diagram.* Fill out diagram and make careful estimate of area burned. Order a normal dose of morphine if patient is conscious and in pain and not intoxicated.

Send to Shock Room if patient is in shock, if area is 25 per cent or more or if there is any sign of respiratory-tract injury, such as hoarseness, cough or dyspnea.

Send all other cases to operating floor.

Notify a surgical service concerning the case, giving all data found on examination above. All patients should be admitted to a surgical service except those with respiratory-tract injury only. The latter group should be admitted to a medical service.

Notify the Aural Service of all respiratory-tract injuries for aural consultation.

DUTIES OF THE SURGICAL SERVICES

See patient at once. Shock may be expected shortly, if not already present, in cases of infants up to six years old with an 8 per cent burn or more and children and adults with a 15 per cent burn or more.

General

(Occasional sick or very feeble patients may have shock with smaller burns.) All burns of these extents should have prompt intravenous treatment even if the temperature, pulse, respirations, blood pressure and hemoglobin level are normal. Do hemoglobin and urine examinations (catheterize if necessary). Repeat blood-pressure and pulse determinations every half-hour. Record all findings.

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Shock

Treat shock or give preventive treatment for shock before dressing the burn. Intravenous electrolyte should be started first, and in all cases in which the areas given above are involved plasma should be given simultaneously.

The electrolyte should consist of the following: 10 per cent dextrose in saline solution with the three following items added per liter: sodium bicarbonate, 3.75 gm (put up in 50-cc ampules), ascorbic acid, 1 gm, and vitamin B complex, 2 ampules. The amounts to be given are shown in Table 1. If the patient is intoxicated or in delirium tremens use five times this dose of ascorbic acid and of Vitamin B complex.

The first dose of plasma should be given rapidly and the first dose of electrolyte slowly unless the patient is in actual shock. If the usual peripheral veins are not accessible or are collapsed, the fluids should be given into the femoral vein, even if the groin region is burned.

It is essential to filter the plasma through sterile gauze just before using and give it through a Murphy drip set, to observe the rate of flow. The amounts to be given are shown in Table 1.

These doses may suffice for burns of 15 to 25 per cent in adults and of 8 to 15 per cent in infants who are not in shock, but in all cases of this severity or greater the systolic blood pressure and hemoglobin must be followed. If the

TABLE 1 First Dose of Electrolyte and Plasma according to the Weight of the Patient

WEIGHT	10% DEXTROSE ELECTROLYTE IN SALINE SOLUTION	PLASMA
lb	cc	cc
150 or more	1500	750
100-149	1000	500
50-99	500	250
35-49	250	150
20-34	150	150
5-19	5 per lb	10 per lb

patient goes into shock with the blood pressure below 70 at any time, the first dose of plasma should be repeated at once or a double dose given rapidly if none has been given. The second and subsequent hemoglobin values will indicate the need for further electrolyte and plasma in the severer cases. Do not give more electrolyte and plasma except for shock unless the hemoglobin has risen ten points or has gone above 110 per cent, whichever is reached first. The second and all subsequent doses of electrolyte and plasma

*These ampules should contain in one ampule 10 mg of thiamin, 4-10 mg of riboflavin, 50-250 mg of niacinamide, 5-10 mg of pyridoxine and 5-50 mg of pantothenic acid. Among the preparations meeting these standards are Betalin Complex (Lilly), Solu B (Upjohn) and Betasynplex (Winthrop).

should be given as outlined in Table 2. Use 10 per cent dextrose in distilled water instead of saline solution during the remainder of the first twenty-four hours.

Further doses are to be given if indicated by further rises in hemoglobin. If further intravenous treatment is needed for shock after an amount of 10 per cent dextrose in distilled water has been given equal to the original dose.

TABLE 2 Subsequent Amounts of Electrolyte and Plasma to be Given for Each Point Rise in Hemoglobin or for Each Point It Is above 100 Per Cent According to the Weight of the Patient

WEIGHT	10% DEXTROSE ELECTROLYTE IN DISTILLED WATER	PLASMA
R	"	"
150 or more	50	0
100-149	35	5
50-99	20	20
35-49	15	15
20-34	10	10
5-19	0.5 per lb	0.5 per lb

of saline solution, give only plasma. Severe burns may need about 1000 cc. of plasma for each 10 per cent area of burn up to a maximum of 5000 cc. in twenty-four hours.[†]

The blood pressure determinations should be continued every half-hour for twenty-four hours, the hemoglobin every two hours until stabilized and the temperature and respiration every two hours. Children under six should have a rectal temperature every hour.

Dressing

A dressing should be applied as early as is consistent with the patient's condition. It should not be started until shock is relieved or until preventive treatment for shock has been started. The intern or resident doing the dressing must be scrubbed, gowned, capped and masked. If the dressing is difficult (25 per cent area or more or a restless or delirious patient), there must also be a scrubbed assistant. The patient should be placed on a sterile sheet and the adherent clothing removed. Blisters must not be cut or broken, and no attempt should be made to wash or clean off any dirt of any kind. A pressure dressing should be applied. Casts may be applied to extremities on direction of a visiting surgeon. The only exceptions to the above are in the cases of the face, neck, anus and genitalia, which should be covered with a thick layer of sterile vaseline and one layer of fine mesh gauze, and nothing else. Provision should be made for replacing these frequently on the ward.

Technic of Pressure Dressing

Under operating-room conditions, fine meshed gauze, dry, should be applied directly to the wound surface. Over this, sufficient Surgine* should be wrapped to make possible even compression by means of an elastic bandage. (The final dressing after compression should be about 2.5 cm. thick.) It should be emphasized that to be maximally effective the dressing should be applied as soon as permitted by the general condition of the patient, since the greatest amount of swelling occurs in the first few hours following injury. Also, since the swelling is not limited to the burned areas but occurs also in the immediately adjacent areas, these areas must be incorporated in the dressing. In burns of the extremities the dressing must extend distally to cover completely the hand and foot, even if these areas are not burned, otherwise, the venous return from these areas will be obstructed, and as the back pressure builds up, the arterial blood supply will be impaired. In certain cases where these precautions have not been taken dressings have had to be removed because of impending gangrene. Elevation of an extremity, with a properly applied dressing, may help prevent stasis and discomfort. In applying a pressure dressing the tension must be uniform, and care must be taken that no more pressure is used than required. In burns of the chest and

abdomen a pressure dressing, as such, cannot be applied without interfering with the patient's breathing, under these circumstances a firm bulky dressing without pressure is used. The initial dressing is left in place for about fourteen days. At the end of this time superficial second-degree burns are healed, while deep burns are beginning to slough.

Post-Dressing Care

Order patient sent to the ward only when well out of shock.

Order morphine in small doses.

Order pulse, respiration and blood-pressure determinations every half-hour.

Order hemoglobin determinations every two hours.

Order temperature determinations every two hours, or every hour (rectal) up to six years old.

Order report of any fall in blood pressure of 20 points or below 90 systolic, any rise in pulse of 30 points or above 120, any rise in respiration above 30 and any rise in temperature to or above 103°F or any chill or other unfavorable symptom.

Post-Dressing Shock

The treatment of this should be mainly by plasma and electrolyte, as directed above. The best sign that shock is fully relieved is a good flow of urine. Be careful of giving too much fluid, especially to very young or very old patients.

Kidney Function

Impairment of kidney function is one of the important early complications of the severely burned patient. To determine the kidney function, urine specimens are necessary, therefore, put all patients with burns of 25 per cent or greater on constant drainage for the first few days. The important etiologic factors of reduced renal function appear to be shock and hemoglobinuria. Every effort must be made to prevent the occurrence of shock or, if shock is present, to combat it vigorously and immediately. Hemoglobinuria is the result of marked hemoglobinemia, which in turn results from injury to the circulating red cells by heat at the time of burning. From analogy with hemolytic blood-transfusion reactions, prompt and continued alkalization of the urine during the period of hemoglobinemia (usually forty-eight to seventy-two hours) should be made. This can be accomplished initially by the intravenous injection of an ampule of sodium bicarbonate, in addition to that already recommended in the section on the treatment of shock. Later, additional bicarbonate should be given only if the urine fails to become or to remain alkaline.

Daily intake and output records should be kept for at least the first week in all patients with burns of 10 per cent or greater, and as much longer as is indicated in patients showing any impairment of renal function. An attempt should be made to keep the urine output between 1000 and 1500 cc. daily. Fluids during the first day should be given as outlined previously. If thereafter the oral intake is insufficient, it should be supplemented by intravenous fluids or by dialysis. No more than 1500 cc. of the supplemental fluids should be electrolyte. In cases with marked oliguria or anuria, care should be taken not to overload the patient, particularly with sodium salts. Plasma protein, nonprotein nitrogen, carbon dioxide, chloride and routine urine determinations should be frequently done.

Hyperpyrexia

Patients with burns frequently have a period of high temperature (up to 109°F) in the first two days after the burn, and not infrequently at much later dates. This is likelier if shock has been poorly treated but can occur without any shock. It is not necessarily the result of infection or of pyrogens in the intravenous fluids.

The patient with a burn does not tolerate a high temperature and will die if it remains at or above 105°F for a few hours. In most cases this fever may be brought down by energetic treatment given at once. If the fluids given have not been according to the above standards, more fluid will help, but main attention should be paid to ice-water sponge baths to all exposed skin. If less than 50 per cent of skin is exposed, it may be necessary to remove some of the dressings. Open windows, create a draft, strip off all bedclothes and make an ice-water bath in the pa-

*Surgine is the name of a composite cotton dressing material used in many hospitals for abdominal pads. Large sterilized rolls of this material are convenient for dressing large burns.

†Whole blood has recently been found to be at least as useful as plasma in the prevention of burn shock. When whole blood is used in large quantities the hematocrit and hemoglobin values are unreliable indicators of blood volume.

tient's bed and keep sponging him for half an hour or more if necessary to bring the temperature down to 102°F. Heated cradles are not to be used at any time in the care of burns. Heavy blankets are to be used only temporarily during a chill or when the room is extremely cold.

Respiratory-Tract Injury

Respiratory-tract injury is a serious complication of burns. Its presence should be suspected in any patient with flame burns of the face (even minor), particularly if he gives a story of inhaling large quantities of smoke and so forth or having lost consciousness. An aural consultation should be obtained immediately on such patients, particular attention being paid to the epiglottis and vocal cords. The room should be humidified, and a tracheotomy set should be kept at the patient's bedside. Respirations should be checked every half-hour. If any hoarseness, dyspnea or stridor occurs, the patient should be placed in an oxygen tent. If there is evidence of bronchial spasm, aminophyllin intravenously or adrenalin or ephedrin by nebulizer should be tried. If signs of laryngeal obstruction develop, immediate tracheotomy must be done. Suction through the tracheal tube should be carried out when needed. An aural consultant should be on hand to perform bronchoscopic aspiration if further obstruction develops. All personnel coming in contact with the patient should be masked.

Sedation. Restlessness may be due primarily to oxygen lack, in which case measures to increase oxygen supply as outlined above should be carried out, to pain (from surface burns), in which case Demerol, rather than morphine, should be used, or to fear and nervousness, in which case barbiturates are indicated.

Chemotherapy. Parenteral penicillin, 25,000 units intramuscularly every three hours, should be started on entry. If the urine output is good, sulfadiazine in full doses may also be given.

Local measures. If burns of the nose and pharynx are present, the patient may be made more comfortable by swabbing the nose with a bland oil and having him gargle with a soothing mixture, such as dextrose in water.

Anemia

After the second day anemia may be troublesome. Make hemoglobin determinations daily until stabilized, and then weekly until discharged. Give whole-blood or red-blood cells in sufficient amounts to keep the hemoglobin at 90 per cent. Any level below 80 per cent should be corrected at once.

Nutrition

Loss of weight, often marked, has long been recognized as a serious complication in severely burned patients.

The estimation of the status of a burn patient with regard to the presence or degree of nutritional deficiency is not simple. The factors necessary for a critical evaluation are the optimum weight of the patient, the observed weight of the patient, the plasma protein level, the plasma albumin level, the plasma volume, the nitrogen intake and the nitrogen output. Actually, main reliance in clinical work has to be placed on a nutritional history, on the patient's weight and on serum protein determinations.

The weights of these patients may be secured at each dressing change by putting the patient, covered with a sterile sheet but with the dressings removed, on a weighed stretcher, each end of which is placed on a scale. Slight changes of weight are often the first indication that the patient's nutritional condition is getting better or worse.

The food provided must be an adequate metabolic mixture containing, in addition to adequate amounts of protein, sufficient calories, fat, carbohydrate, minerals, water and accessory food substances. As seen in Table 3, the minimum essential needs for protein, calories and vitamins are as great as or greater than the need for these items in an illness of any kind. This table is to be followed for adults and for children weighing 50 pounds and over. Reduce by 25 per cent from thirty to forty-nine pounds, and by 50 per cent from fifteen to twenty-nine pounds. Under fifteen pounds give 125 per cent, 150 per cent, 200 per cent and 300 per cent, respectively, of normal pro-

teins and calories for 1-4, 5-9, 10-19 and 20+ per cent burns. Give 25 per cent of vitamins indicated for the area in above table to these infants.

Additional vitamins from liver and yeast are helpful. Severe cases should be given up to 30 gm of yeast a day. Liver may be given in the form of liver extract.

Whenever possible, protein losses or deficiencies should be corrected by oral feeding. It is not enough for the surgeon to order a high-protein, high-calorie, high-vitamin diet. If such a diet is ordered, the patient may fail to benefit from the order for any one of the following reasons. The diet presented to the patient is not as specified. The

TABLE 3 *A Minimum Food Needed Daily by Patients with Burns, according to Total Area Unhealed*

BURN AREA	PROTEIN	CALORIES	ASCORBIC ACID	THIAMIN	RIBO-FLAVIN	NICOTIN AMIDE
%	gm		gm	mg	mg	mg
20	300-400	5000	2.0	50	50	500
10-19	200	3500	1.0	25	25	200
5-9	125	3000	0.5	15	15	100
1-4	90	2500	0.5	10	10	50

diet presented is not eaten in whole or in part because it lacks palatability, there is lack of appetite, and there is a lack of nurses to encourage eating. Food eaten may be partly or wholly lost because of diarrhea or vomiting.

These difficulties have been frequently encountered in caring for patients with burns during the last two years. The fact that the first item is mentioned may be a surprise. What especially happens in these days with the shortage of nurses is that there are frequent times when supplementary feedings are not brought to the patient because the nurse has other duties to perform that she thinks are more important or more urgent. This is particularly likely to happen at night.

The three items listed under the second item are interrelated. It is a common experience to find that a sick patient has no appetite. If, however, special attention is paid to the likes and dislikes of the patient and special or other nurses are available to encourage eating and to offer meals when the patient desires them instead of only at stated routine times, many such patients will eat a surprisingly large amount of food.

The two items under the third item are also related to each other. Forcing the diet on a sick patient does not always result in a net gain. Nausea, vomiting, distention and diarrhea, singly or together, are limiting factors. In general, the sicker the patient is the less fat is tolerated and the larger the proportion of protein should be. It has been found that at least 25 per cent of the calories in the diet should come from protein and not over 15 per cent from fat if any of these intestinal symptoms have recently occurred. It is well to take a number of days to increase the food intake, since sudden increases are likelier to be followed by gastrointestinal symptoms, which can usually be avoided by more cautious increases. If this diet is not tolerated, protein in the form of a digest should be tried and will frequently be well tolerated. The available digests are not particularly palatable and should generally be given by intubation.

Intubation feeding is important and may be used to increase greatly the intake of food. Medium-caliber nasal stomach tubes are used and left in all the time or for many hours a day. If left in continuously, the tube should be removed every third or fourth day for cleaning. About 200 cc of fluid may be given at a time, spaced between meals and at night, but there is a wide variation in the amount and frequency of supplementary tube feedings that different patients can take. It is well to start with a mixture of half skim milk and half water or one of protein hydrolysate and carbohydrates. Instead of supplying the mixture in intermittent doses, a drip apparatus may be used that can, after a short period of training, be regulated by some patients themselves. If 125 to 150 gm of protein and 2000 to 2500 calories are given by intubation in addition to an average house diet, the patient should receive a total of about 200 gm of protein and over 4000 calories. Usually, however, the patients who are

given forced supplementary feeding will not take the whole of their house diet in addition

In certain patients needing only moderately high diets and in nearly all those needing 300 gm of protein or sugar, it may be impossible to furnish the required foodstuffs by the oral or gavage route. In these cases supplemental intravenous feedings are indicated. Intravenous feedings are also indicated in cases of disturbed gastrointestinal function, either primary or secondary to nutritional disturbance. In the latter cases there may be surprising improvement in gastrointestinal function after intravenous alimentation.

Parenteral feeding should be continued as a supplement until oral feeding, with or without gavage, has been established at a sufficient level not only to maintain the patient in nutritional equilibrium but also to restore at a rapid rate all tissues that have been depleted. Up to 225 gm of protein equivalent have been given in twenty-four hours in the form of an acid hydrolysate of casein (Parenamine) or an enzymatic hydrolysate of casein and pancreas (Amigen). The suggestion of Butler and Talbot² for increasing the value of intravenous protein hydrolysates by adding dextrose has been successfully followed. By adding 300 cc of 50 per cent dextrose to 1000 cc of Amigen, there is obtained 1500 cc of a solution composed of 4 per cent hydrolysate and 15 per cent dextrose, which represents 50 gm of protein and 1000 calories. This quantity can be given into a large vein with a 20-gauge to 21-gauge needle in four hours, without much danger of thrombosis of the vein and can be repeated three times a day. The speed of administration is limited by the amount of dextrose present, the ratio of dextrose administration not exceeding 0.8 gm per kilogram of body weight per hour. Administration at a faster rate produces glycosuria and excessive diuresis. Nausea may be caused if the enzymatic hydrolysate is introduced too rapidly, and thrombosis of the vein used for the injection may occur with the acid hydrolysate.

In late stages of severe burns, testosterone propionate should be given in doses of 25 mg intramuscularly every other day to increase the positive nitrogen balance by reducing the loss of nitrogen in the urine.

Subsequent Dressings and Grafts

These should be done infrequently, about ten to fourteen days apart, and in the operating room under strict asepsis.

The dressings should be large, bulky and firm. Until some antiseptic of value is found, no ointments and no chemicals should be used except on the face, neck, genitalia and anus. The ointment dressings on these areas alone should be done whenever necessary, and therefore frequently, on the ward. Skin grafts should be placed on all deep burns at the earliest possible time. Frequent dressings and surface antiseptics are not needed and should not be used before grafting. The dressings outlined above are the best possible preparation for grafting. If hemolytic streptococci are found, intramuscular penicillin should be used before and after grafting in doses of 20,000 units every two hours. In the absence of the streptococcus penicillin is not necessary. Dermatome grafts should be employed whenever possible. When general anesthesia is needed for grafting or for dressings the anesthetic of choice is cyclopropane.

NURSING CARE

Even in spite of carrying out every item in this outline, the fact remains that a patient with a deep burn of 5 per cent or more can be saved only if special nursing care is given. This is not at present provided on the wards of many hospitals unless special nurses are available. Any patient with an unhealed deep burn of 20 per cent or more needs three nurses a day, with one of 10 to 19 per cent, two periods of special nursing a day are needed, and with one of 5 to 9 per cent, one period of special nursing a day is needed.

A full discussion of the present status of the treatment of burns has been published and explains the reasons for the directions given here.³

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EFFERVESCENT MIXTURES AS ADJUVANTS TO THE RAPID ABSORPTION OF INGESTED DRUGS*

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ALTHOUGH there are many and obvious advantages to the oral administration of drugs, there are certain equally obvious disadvantages. Of these the most prominent are the uncertain and variable rate of absorption and gastric irritation. It is probable that when irritation occurs, its intensity varies with the duration of the contact of the drug with the gastric mucosa, and that it is least when emptying of the stomach is rapid. Since few drugs are absorbed directly from the stomach, the rate of emptying affects the speed of therapeutic response, and for drugs whose action depends on concentration developed in the blood,—for example, salicylates and sulfonamides,—the rate of emptying affects the extent of the therapeutic effect derived from a single dose. Any adjuvant procedure that prevents delay in the emptying of the stomach and obviates variations in the rate of emptying overcomes, at least partially, some of the handicaps of oral therapy. This fact has special importance for drugs which in themselves may delay emptying, as may large doses of acetylsalicylic acid, as has been shown by Schnedorf, Bradley and Ivy.¹

The study presented here extends the investigations of these authors on the effects of salicylates on the rate of emptying. It further deals with the relation between the rate of emptying and the concentration of drugs developed in the blood and with the influence of acids, alkalies, carbon dioxide and effervescent mixtures on the rate of emptying of the stomach and speed of absorption.

INFLUENCE OF SALICYLATES ON RATE OF GASTRIC EMPTYING

Schnedorf, Bradley and Ivy have reported delay in emptying of the stomach after oral doses of 1 and 2 gm of acetylsalicylic acid. To determine whether this delay was due in part to the systemic effects of absorbed salicylate, the emptying time was determined in a series of rats to which the salicylate was administered intravenously. The rate of emptying was evaluated from the percentage retention at two hours of a test meal of 25 per cent solution of dextrose, to the amount of 2.5 gm of dextrose per kilogram of body weight. Thirty-nine rats were used—30 as experimental animals and 9 as controls, which received injections of saline instead of the salicylate solution. Thirty minutes after the injection of sodium salicylate or saline solution the test meal was

given. Two hours later the animals were anesthetized with sodium amytal, the abdomen was opened, and the stomach was quickly tied off and removed. The amount of unabsorbed dextrose in the stomach contents was determined by the method of Shaffer and Somogyi.² The findings are presented in Table 1.

TABLE 1 *Influence of Intravenous Administration of Salicylate on Rate of Emptying of Stomach in Rats*

AMOUNT OF SALICYLATE gm/kg	NO OF ANIMALS	DEXTROSE RECOVERED FROM STOMACH	
		EXTREMES	AVERAGE
None	9	0-5	2
0.05	8	1-5	2
0.10	8	2-39	14
0.25	6	31-78	43
0.50	8	55-78	66

The gastric emptying was not influenced by small doses of salicylate but was markedly delayed by the systemic action of large doses. For doses of 0.05 gm per kilogram, there was no appreciable delay in emptying time and the retention at two hours averaged only 2 per cent, but with doses of 0.5 gm, 66 per cent of the test meal was still in the stomach at two hours.

The larger doses and correspondingly high concentrations of salicylate in the blood have significance in the therapy of rheumatic fever but none for the use of salicylates for analgesia. To determine the possible effects on gastric emptying of the local action of salicylates on the gastric mucosa in the presence of low concentrations in the blood, as in ordinary analgesic doses, a series of determinations was made on 3 normal human subjects. They were given 0.6 gm of acetylsalicylic acid and 100 cc of water and, in control experiments, water but no salicylate. The rate of emptying was determined by fluoroscopic examination at intervals of fifteen minutes, using the test meal and technic developed by Van Lière and Sleeth.³ The average times were obtained from a number of observations made at intervals of several days. For Subject 1 the average, when water alone was given, was two hours and fifteen minutes and after acetylsalicylic acid, two hours, for Subject 2 the corresponding values were one hour and forty-five minutes and two hours, for Subject 3, they were two hours and one hour and forty-five minutes. It appears that this salicylate has, in ordinary doses given for analgesia, no delaying action from local or systemic effects on the rate of gastric emptying.

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INFLUENCE OF ACIDS, ALKALIES AND EFFERVESCENT MIXTURES ON RATE OF GASTRIC EMPTYING

A comprehensive review of the influence of acids and alkalies on the rate of emptying of the stomach will be found in the writings of Van Lière and Sleeth.⁴ In spite of conflicting results the well substantiated findings are as follows. Strong acids inhibit gastric motility, whereas weak acids have an undetermined effect, and moderate amounts of sodium bicarbonate hasten and large amounts slow the emptying time. There is no full agreement among investigators concerning the mechanism involved. Van Lière and Sleeth suggest three hypotheses: an effect on the action of the pylorus, an effect on the secretory activity of the stomach followed by changes in motility and a direct effect on gastric motility. Objections can be raised against all three of these explanations.

In the experiment reported herein 3 normal human subjects were used. The rate of gastric emptying after a test meal, as described above, was determined at intervals of several days. In a series of control determinations made with water administered ten minutes after the test meal, it was found that the rate of emptying for each subject was fairly uniform. The water was replaced on separate occasions by an equal volume of fluid containing 1.5 gm of tartaric acid, 2.0 gm of sodium bicarbonate or an effervescent mixture of 1.5 gm of tartaric acid and 2.0 gm of sodium bicarbonate. Three determinations were made on each subject for each of the materials administered. The findings are given in Table 2. As seen from this table

TABLE 2 *Influence of Tartaric Acid, Sodium Bicarbonate and an Effervescent Mixture on the Rate of Emptying of the Stomach*

SUBJECT No.	GASTRIC EMPTYING TIME			
	CONTROL	AFTER SODIUM BICARBONATE	AFTER TARTARIC ACID	AFTER EFFERVESCENT MIXTURE
1	2 hr	1 hr	1 hr 45 min.	1 hr., 15 min
	2 hr	1 hr	2 hr	1 hr.
	2 hr	1 hr 30 min.	2 hr	1 hr
2	1 hr., 30 min.	1 hr	2 hr.	1 hr
	1 hr., 30 min	1 hr	1 hr., 30 min	45 min
	1 hr 45 min	45 min	1 hr., 45 min	45 min
3	1 hr 30 min	45 min.	1 hr 45 min	45 min
	1 hr., 30 min	1 hr	1 hr., 30 min	45 min
	1 hr 45 min	1 hr 15 min	2 hr	45 min

the rate of emptying was not appreciably influenced by tartaric acid but was markedly shortened by sodium bicarbonate and by an effervescent mixture of the two substances. These findings will be discussed later.

To avoid continual fluoroscopic procedures and to check the validity of the data obtained by fluoroscopy, the rate of gastric emptying was determined by direct measurement. By means of a Levin tube the stomach contents were withdrawn at intervals and, after the volume had been determined, re-

injected into the stomach. Each subject was trained to pass the tube without assistance, after a few days of practice nausea and apprehension which might affect gastric motility, disappeared. A bouillon test meal was used.

The subjects received their last meal at dinner the day previous to each experiment and no fluid after midnight. At 9 a.m. the tube was passed and the small amount of gastric juice present in the stomach was withdrawn for preliminary determination of the hydrogen-ion concentration. Bouillon was then swallowed and immediately thereafter 100 cc of the solution under study. The tube was left in place for the duration of the experiment. At intervals of fifteen minutes the stomach contents were withdrawn as completely as possible and measured. A few cubic centimeters was retained for measurement of the reaction and the remainder was returned to the stomach.

That repeated withdrawal and return had no appreciable influence on the rate of gastric emptying was shown by comparative determinations in which the stomach contents, on one occasion, were removed and returned as described and on another were allowed to remain for an hour before removal. The values obtained are shown in Table 3.

At intervals of several days two additional determinations were made on the two subjects, using 100 cc of bouillon and 100 cc of water. The findings

TABLE 3 *Volume of Stomach Contents with Single and Repeated Withdrawals*

SUBJECT No.	VOLUME OF STOMACH CONTENTS			
	15 MIN	30 MIN	45 MIN	60 MIN
1	cc 160	cc 140	cc 130	cc 120
	—	—	—	110
2	18"	180	140	90
	—	—	—	105

are given as the first four values in Table 4. As seen, the residuum at one hour was substantially the same as in the determinations recorded in Table 3.

Again at intervals determinations were made after the subjects were given the following: 100 cc of bouillon and 100 cc of effervescent mixture containing sodium bicarbonate (4 gm) and tartaric acid (3 gm), but with the mixture boiled to remove all free carbon dioxide and subsequently cooled, 100 cc of bouillon and 100 cc of effervescent mixture, not boiled but with active effervescence, and 100 cc of bouillon and 100 cc of carbonated water. The findings are given in Table 4. As seen, the effervescent mixture, unboiled, hastened the emptying of the stomach with a residuum averaging 20 cc at sixty minutes, as compared to 100 cc for the control experiments. A comparable hastening effect resulted when carbonated water was used instead of the effervescent mixture. A moderate hastening

effect resulted when the effervescent mixture was boiled prior to administration. Under the conditions of these experiments there appeared to be no correlation between the hydrogen-ion concentration of the gastric juice and the extent of gastric emptying.

Tartaric acid was used in this experiment rather than citric acid, which is often employed in effervescent mixtures, to avoid any effects from possible systemic alkalization due to the oxidation of the citric acid. Tartaric acid in doses of 15 gm has no effect on gastric emptying.

The fact that carbonated water hastens gastric emptying confirms the work of Carnot and Koskowski,⁵ Kussmaul,⁶ Jaworski⁷ and Binet and Lebon.⁸ In addition, it casts some light on the pos-

small and large doses of sodium bicarbonate. In the presence of a normal gastric acidity, a small dose of sodium bicarbonate hastened the emptying of the stomach. In subjects with a hyperchlorhydric response to the test meal, the same dose of sodium bicarbonate caused an even greater hastening in gastric emptying. In those with an achlorhydric response, it had no effect on the rate of emptying. The interpretations made of these findings, in the light of the work presented here, are as follows. In the presence of a normal amount of hydrochloric acid in the gastric juice, the ingestion of moderate amounts of sodium bicarbonate causes liberation of carbon dioxide, with consequent hastening of gastric emptying. In the absence of hydrochloric acid, carbon dioxide cannot be liberated and there is con-

TABLE 4 *Volume and Hydrogen-Ion Concentration of Stomach Contents after Various Types of Effervescent Mixtures*

SUBJECT No	PROCEDURE	VOLUME OF STOMACH CONTENTS				pH OF STOMACH CONTENTS					
		15 MIN	30 MIN	45 MIN	60 MIN	0	15 MIN	30 MIN	45 MIN	60 MIN	
1	Bouillon, 100 cc, and water, 100 cc	200 160	140 140	125 130	110 110	4.5 2.5	5.8 3.9	4.1 2.2	2.6 1.6	1.85 1.3	
2	Bouillon 100 cc, and water, 100 cc	180 220	170 160	140 120	70 110	3.1 2.5	4.0 4.5	2.8 3.6	2.6 2.0	2.2 1.5	
1	Bouillon, 100 cc, and effervescent mix tore boiled 100 cc.	150 145	150 110	100 60	40 60	2.5 4.3	4.6 6.2	3.0 4.6	2.0 1.4	1.6 1.6	
2	Bouillon 100 cc, and effervescent mix tore boiled 100 cc.	160 180	100 130	50 90	45 40	— —	6.1 6.8	5.8 6.6	4.3 5.0	1.8 3.8	
1	Bouillon 100 cc. and effervescent mix tore, 100 cc.	140 145	40 60	30 30	20 30	2.8 3.2	5.8 6.0	2.4 1.9	1.5 1.5	1.4 1.5	
2	Bouillon 100 cc, and effervescent mix- tore, 100 cc.	85 185	25 120	15 65	0 30	— —	5.9 —	3.2 —	1.4 —	1.4 —	
1	Bouillon, 100 cc, and carbonated water 100 cc.	175 165	125 50	75 30	30 15	2.6 —	2.8 —	1.8 —	1.8 —	1.8 —	

sible mechanisms of effervescent mixtures in general. In the experiments reported herein the effect of the effervescent mixture on gastric emptying did not disappear completely after boiling to remove the carbon dioxide from the effervescent mixture. The relative amounts of sodium bicarbonate and tartaric acid in the mixture used were such as to leave an excess of about 1 gm of bicarbonate after boiling. Such an amount does not seem sufficient to account for the effect observed, which may have been due in part to sodium tartrate. From experiments, to be described later, there is evidence that sodium tartrate hastens gastric emptying. Van Lière and Sleeth⁴ have shown that disodium phosphate has this effect.

The greater effect of the unboiled effervescent mixture as compared to the boiled is undoubtedly connected with the liberation of carbon dioxide, which plays a predominant role in shortening gastric emptying following administration of effervescent mixtures. Sodium bicarbonate in normal healthy subjects exerts an action substantially the same as that of the effervescent mixture, and it is our opinion that it acts mainly through the liberation of carbon dioxide by reaction with the hydrochloric acid of the gastric juice.

Shay and Gershon-Cohen⁹ investigated the rate of gastric emptying following administration of

sequently no hastening of gastric emptying. When large amounts of bicarbonate are given only a part reacts with hydrochloric acid in the normal subjects, and it is possible that the large amount of residual alkali counteracts the effects of the carbon dioxide. In hyperchlorhydric subjects, as shown by Shay and Gershon-Cohen, an increased rate of emptying occurs even when large amounts of bicarbonate are given, a result that may possibly be attributed to the greater evolution of carbon dioxide and lesser residual alkali.

If this interpretation of the data of Shay and Gershon-Cohen is correct, the role played by carbon dioxide in hastening gastric emptying seems significant not only when carbonated water is administered but also when sodium bicarbonate and effervescent mixture are given. It should be emphasized that when bicarbonate alone is used in a normal subject, the need is for moderate rather than large doses, and that the effectiveness in hastening gastric motility is, in large part, conditioned on the presence of hydrochloric acid in the stomach.

INFLUENCE OF GASTRIC EMPTYING TIME ON ABSORPTION OF DRUGS

The concentration of sulfathiazole in the blood was determined in 2 subjects at intervals after taking 0.25, 1.0 and 3.0 gm of the drug, with and with-

out an effervescent mixture consisting of sodium bicarbonate and tartaric acid. The findings are shown in Table 5. The use of the effervescent mixture favors a high concentration in the blood in the early phase of absorption, which is especially marked with the small and moderate doses.

Rapid absorption with an earlier rise of the concentration of the drug in the blood is perhaps of less specific therapeutic importance with a drug such as sulfathiazole, with which prolonged maintenance

The most striking feature is the higher concentration of salicylate in the blood up to two hours for doses of 0.6 gm and to four hours for doses of 1.6 gm when given with various adjuvants. The effervescent mixture was the most effective in increasing the concentration. The increase in concentration signifies a definite benefit in rapid therapeutic action.

These experiments appear to indicate that small amounts of markedly alkaline salts hasten the

TABLE 5 Blood Concentrations of Sulfathiazole following Its Ingestion with and without an Effervescent Mixture

Subject No	CONDITION	CONCENTRATION OF SULFATHIAZOLE					
		DOSE gm	½ HR. mg/100 cc	1 HR. mg/100 cc	1½ HR. mg/100 cc	2 HR. mg/100 cc	
2	After breakfast	No effervescent mixture	0.25	0.04	0.24	0.33	—
			0.25	0.06	0.10	0.22	—
	With effervescent mixture		0.25	0.20	0.32	0.58	—
			0.25	0.19	0.50	0.43	—
	1	No effervescent mixture	3.0	1.88	—	4.60	4.93
		With effervescent mixture	3.0	1.55	—	4.90	5.68
1	Before breakfast	No effervescent mixture	0.25	0.30	0.55	0.76	—
			0.25	0.90	0.66	0.53	—
	With effervescent mixture		1.0	0.31	—	—	1.42
			1.0	1.36	—	—	1.54

of concentration is desired, than with acetylsalicylic acid used as an analgesic, with rapid action as a desideratum. It should be borne in mind, however, that the more rapid emptying correspondingly limits the possible gastric irritation from the drug.

Similar experiments carried out with acetylsalicylic acid were intended not only to determine

emptying time of the stomach irrespective of the production of carbon dioxide, that carbon dioxide alone hastens gastric emptying, and that in interpreting the action of an effervescent mixture the following factors enter into consideration: the carbon dioxide produced, the weak alkaline salts formed from the reaction inducing the effervescence and

TABLE 6 Blood Concentrations of Salicylic Acid following the Ingestion of Acetylsalicylic Acid with and without Other Substances.

Subject No	CONDITION	DOSE OF DRUG gm	CONCENTRATION OF SALICYLIC ACID			
			½ HR. mg/100 cc	1 HR. mg/100 cc	2 HR. mg/100 cc	4 HR. mg/100 cc
2	Drug alone	0.6	0.80	1.80	3.80	2.65
	Drug and effervescent mixture	0.6	4.33	4.10	3.53	2.20
	Drug and sodium citrate (4 gm)	0.6	4.25	4.06	3.87	2.60
	Drug and sodium tartrate (4 gm)	0.6	1.40	3.00	3.35	2.74
	Drug and carbonated water	0.6	1.80	3.50	3.80	2.33
	Drug alone	1.6	1.67	3.67	5.53	7.33
1	Drug and effervescent mixture	1.6	—	8.93	10.20	10.30
	Drug and sodium citrate (4 gm)	1.6	3.00	4.06	6.00	9.20
	Drug and sodium tartrate (4 gm)	1.6	4.47	5.86	10.01	8.40
	Drug and carbonated water	1.6	2.53	3.86	8.34	9.85

the influence of the effervescent mixture on emptying of the stomach but also to clarify the part played by the carbon dioxide liberated and by the salts formed from the effervescent mixture. Acetylsalicylic acid in doses of 0.6 and 1.6 gm was given to 2 fasting subjects with an effervescent mixture of tartaric acid (3 gm) and sodium bicarbonate (4 gm) with sodium citrate (4 gm), with sodium tartrate (4 gm) and with carbonated water (150 cc). The findings are given in Table 6.

the alkalinity that may occur from an excess of bicarbonate.

CONCLUSIONS

Attempts at hastening the rate of gastric emptying seem warranted when a quick effect of a drug orally administered is required with minimum irritation of the stomach. Such attempts seem further justified by the possibility that some drugs delay gastric emptying when given in large amounts.

Evaluation of the rate of gastric emptying by means of fluoroscopic examination, gastric intubation and determinations of blood concentrations of test drugs indicates that effervescent mixtures decrease the emptying time of the stomach.

The effect attendant on the administration of an effervescent mixture seems to be due in part to the presence of weak alkaline salts and in part to the production of carbon dioxide.

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MEDICAL PROGRESS

NEUROLOGY

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THE significant publications in the field of neurology in 1945 included a number of studies on the physiology of the nervous system, further reports on the use of antibiotics in the infections of the nervous system, including syphilis and tuberculous meningitis, the introduction of a new drug in the treatment of petit-mal epilepsy and articles on various miscellaneous subjects.

PHYSIOLOGY

Two studies on the physiology of the pyramidal tract have been contributed by Lassek.^{1,2} In the first he correlated the occurrence of the Babinski reflex with the other evidence of damage to the corticospinal tract. The material used in this study comprised 1600 case reports collected from the literature in which the Babinski sign was exhibited. The Babinski reflex was present bilaterally in 85 per cent of the 200 cases that showed various degrees of suppression of the somatic nervous activity, such as that occurring in unconscious states. All degrees of motor activity from normal to complete paralysis were found. The signs and symptoms that accompanied the Babinski sign, in the order of frequency, were somatic motor deficit, hyperactive patellar reflex, absence of abdominal reflex, spasticity, ankle clonus, hypoactive knee jerk, absence of cremasteric reflex, flaccidity and patellar clonus.

In the second study, Lassek attempted to determine the frequency of changes in the axones in the pyramids in patients who had evidence of cerebrovascular lesions during life. Sections of the medulla

of 166 such patients were stained by the Davenport method. There was complete destruction of the axones in the pyramids in only 7, and partial damage in 36. No loss of fibers in the pyramids could be demonstrated in 63 cases, although many of these patients had a hemiplegia during life. Lassek concludes that hemiparesis or hemiplegia, caused by chronic cerebral vascular lesions, may occur with little or no destruction of the fibers in the pyramid of the medulla.

Studies in disturbances of the sleep mechanism were made by Davison and Demuth.^{3,4} In 9 patients pathologic sleep was associated with lesions confined to the cortex. Increased intracranial pressure was present in only 4 of these cases, and compression of the hypothalamus was excluded in 7. From their histologic study of the brains of these 9 cases, the authors conclude that some fibers for the cortical control of sleep originate in the cerebral cortex, especially the hippocampal, cingular, frontal and temporal convolutions. In 25 patients with pathologic sleep there was involvement of the corticodiencephalic structures. The hypothalamus was invaded or compressed in 16 cases, and the basal ganglia were involved in 16. The authors state that fibers for the control of sleep, which originate in the cortex, reach the hypothalamus by way of the median forebrain bundle, the fornix and the inferior thalamic peduncle.

The effect on the nerve-action potential of various choline esterase inhibitors was studied by Bullock, Nachmansohn and Rothenberg.⁵ They have found that strychnine, eserine and cocaine reversibly depress the action potential of the giant axone of

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the squid Prostigmine, despite its *in vitro* action on choline esterase, does not affect the action potential because it is a quaternary ammonium and cannot penetrate a lipid membrane. The authors consider their findings to be consistent with the theory that acetylcholine is the depolarizing agent released during the passage of the impulse and that the physiologic role of choline esterase should be the rapid removal of the ester, inhibition of the enzyme should result in enduring depolarization and therefore abolition of conductivity.

The sympathetic dermatomes in the lumbar and sacral regions are outlined by Richter and Woodruff⁶ in 75 patients who had sympathectomies in this region. With the electrical skin-resistance method, the area of increased skin resistance followed a definite segmental pattern that corresponded closely to the sensory and vasomotor dermatomes determined by Foerster.

A new method of determining cerebral blood flow in man is described by Kety and Schmidt.⁷ The method is based on the principle that the rate at which the cerebral venous blood content of an inert gas (nitrous oxide) approaches the arterial blood content depends on the volume of blood flowing through the brain. Comparison of the results with the use of this method with those obtained by the direct measurement of flow in monkeys showed that the gaseous method was quite accurate.

The effect of the administration of phenobarbital or dilantin on the recovery of motor function following ablation of the fourth and sixth cortical areas in monkeys was studied by Watson and Kennard.⁸ Phenobarbital in nonsedative doses retarded the rate of recovery. Dilantin alone had no effect on the rate or recovery of motor function, but dilantin when administered together with doryl inhibited or prevented the enhanced recovery rate that occurs when doryl is given alone.

Richter⁹ reports that degenerative changes can be produced in the basal ganglia of monkeys when the animals are chronically poisoned by exposure to carbon disulfide vapor for many months. The pathologic changes consist of extensive necrotic lesions in the globus pallidus and the substantia nigra. The animals present many of the clinical signs often seen in disease of the basal ganglia in man, but the parkinsonian type of tremor has not been observed.

Bender¹⁰ states that although polyopia and monocular diplopia usually are hysterical symptoms, they may occur on an organic basis. He emphasizes the fact that lesions in the occipital lobe or central visual pathways, as well as lesions in the media of the eye, can be followed by polyopia or monocular diplopia.

Curare was used by James and Braden¹¹ in the treatment of 12 paraplegic patients, injured in war, who suffered with annoying and distracting flexor withdrawal reflexes of the lower extremities. The

use of this drug resulted in a decrease in the frequency and severity of the reflexes, with resulting general improvement.

INFECTIONS

A case of tuberculous meningitis in a one-year-old infant treated with streptomycin is reported by Cooke, Dunphy and Blake.¹² The diagnosis was confirmed by cerebrospinal-fluid abnormalities and by guinea-pig inoculation. The streptomycin was administered intramuscularly and intrathecally. The baby had survived for two hundred and thirty-four days since the start of the treatment. The meningitis was apparently entirely cured, but there were residuals indicating severe damage to the nervous system.

Twenty-eight consecutive cases of influenzal meningitis were treated by Smith, Wilson and Hodes.¹³ The incidence of influenzal meningitis in infancy follows a curve similar to that of pneumococcal meningitis, that is, most cases occur between the ages of three and nine months. Early diagnosis and intensive therapy, with the use both of sulfonamides and of type-specific antibody, reduced the mortality to 7 per cent, which is comparable to that of meningococcal meningitis. The incidence of serum reactions was high but did not militate against its use.

The neurologic complications of meningococcal meningitis formed the subject of reports by Farmer¹⁴ and by Degen.¹⁵ Focal neurologic signs were present in 26 of the 300 patients reported by Farmer. There were 9 cases with sixth-nerve paralysis, 9 with seventh-nerve paralysis, 5 with eighth-nerve paralysis and 3 with transient focal cerebral complications — convulsions, hemiplegia and aphasia. The sixth-nerve paralysis, which was most often unilateral, developed early in the course of the disease, while the cerebrospinal fluid was purulent, and complete recovery usually occurred within a few weeks. The seventh-nerve paralysis, either unilateral or bilateral, was a late complication, developing five to fourteen days after the onset and at a time when the cerebrospinal fluid was relatively cell free. Recovery from the facial paralysis was usually complete within a few months. Eighth-nerve paralysis occurred more frequently in children than in adults. Both eighth nerves were usually involved, and the hearing loss was permanent. A follow-up study of 986 patients with cerebrospinal meningitis was made by Degen.¹⁵ Sequelae of the meningitis were found in 387 patients, 91 of whom were incapacitated. The sequelae included the following: emotional instability, in 109 patients; headache, in 170; backache, in 46; inability to concentrate and poor memory, in 8; total deafness, in 27; impaired vision, in 22; disturbances of vision, in 7; strabismus, in 9; aphasia, in 2, both patients being over fifty years of age; poor balance, in 20; and dizziness, in 13.

The results of the use of penicillin in the treatment of neurosyphilis are reported from several clinics. Gammon and his associates¹⁶ summarize the changes that occurred in the cerebrospinal fluid of 89 patients treated with 1,200,000 to 4,000,000 units of penicillin. The cell count and protein content of the cerebrospinal fluid was reduced to normal in all but 6 patients. The authors conclude that large doses of penicillin, especially when repeated, give the best results.

O'Leary and his co-workers¹⁷ report their results with the use of penicillin in 100 patients with various types of neurosyphilis. The dosages varied from 1,200,000 to 8,000,000 units, and the routes of administration included the intramuscular, intravenous and intraspinal. The clinical and serologic response in patients with meningeal neurosyphilis was excellent, whereas patients with dementia paralytica were improved only slightly, if at all. The combination of penicillin and fever therapy did not improve the results noted from the fever treatment alone. Good results were obtained in reversing the cerebrospinal fluid abnormalities in patients with asymptomatic neurosyphilis who received 1,200,000 units of penicillin in one week in association with either three spinal drainages or intraspinal treatments with penicillin. The authors conclude that the administration of penicillin by the intravenous, intramuscular or intraspinal route is not capable of controlling the parenchymatous forms of neurosyphilis.

Rose¹⁸ reports the results from the use of penicillin in combination with fever therapy in 140 cases of symptomatic neurosyphilis. The treatment consisted of the intramuscular injection of 3,000,000 units of penicillin combined with a short course of fever therapy, half the amount usually prescribed. The results in 36 patients with reasonably early dementia paralytica were improvement in 24, no change in 11 and worsening in 1. There was improvement in only 1 of the 13 cases of long-standing dementia paralytica. No dramatic change was noted in the course of the patients with tabes dorsalis. The progress of the visual loss was arrested in 5 of 6 cases of optic atrophy. The effect of penicillin on the cerebrospinal-fluid abnormalities compared favorably with that of other forms of antisiphilic treatment.

The hazards of administration of penicillin and other substances intrathecally is the subject of three articles. Siegal¹⁹ reports the case of a sixty-six-year-old woman with Type 14 pneumococcus meningitis who was treated with sulfadiazine by mouth and with penicillin by the intravenous and intraspinal routes. The patient recovered from the meningitis but developed a flaccid paralysis, complete sensory loss below the level of the tenth thoracic segment and loss of sphincter control. The neurologic residuals were permanent. A case of meningitis with headache, stiff neck and fever fol-

lowing the intrathecal injection of Pantopaque is reported by Tarlov.²⁰ Biopsy of the meninges confirmed the diagnosis of meningitis. Three cases of spinal arachnoiditis and paralysis following spinal anesthesia are reported by Kennedy, Somberg and Goldberg.²¹

CONVULSIVE DISORDERS

Experiments were made by Forster²² on the effect of acetylcholine on the electrical activity of the cortex of cats. He reported that the electrical discharges thus produced were similar to seizure discharges and were correlated with the muscular components of seizures that followed the application of the acetylcholine to the cortex.

Several new drugs have been tested as anti-convulsants in human beings. Clein²³ reports beneficial effects in grand-mal epilepsy and to a less extent in petit-mal epilepsy by the administration of Hydantal (3-methyl, 5-phenylethyl hydantoin) and phenobarbital. On the basis of 10 cases the author states that Hydantal has all the advantages of previous hydantoin derivatives but is without their toxic effects.

The anticonvulsant activity of sulfoxides and sulfones was tested in animals by Merritt, Putnam and Bywater.²⁴ Several of the phenyl derivatives of these compounds were found to have anti-convulsive activity in animals. One of these, ethyl phenyl sulfone, was given a clinical trial in patients with epilepsy. It was found that this drug had definite anticonvulsive activity in such patients, but this activity was not sufficiently greater than that of phenobarbital or phenytoin sodium to justify its recommendation for general use.

The use of Tridione (3,5,5-trimethylloxazolidine-2,4-dione) in the treatment of epilepsy was reported by Thorne,²⁵ Lennox²⁶ and DeJong.²⁷ Thorne administered Tridione to 11 patients with grand-mal seizures and compared the results with that obtained with previous forms of treatment. There was improvement in 3 patients, no change in the frequency of seizures in 6 and death from extraneous causes during treatment in 2. Lennox describes the clinical and electroencephalographic characteristics of petit-mal epilepsy and reports on the effects of administration of Tridione to 50 patients with petit-mal seizures. The drug was effective in controlling the seizures in 28 per cent and reduced their frequency in 52 per cent. In 10 patients who had occasional or frequent grand-mal seizures in addition to the petit-mal attacks, the administration of Tridione did not control the former. The principal side effect of treatment was photophobia, which affected adults and older children more frequently than it did younger children. DeJong administered Tridione in combination with Phenytoin Sodium, phenobarbital and bromides to 6 patients who were subject to minor epileptic seizures classified under the term "psychomotor attacks." Some of these patients also had

grand-mal and petit-mal seizures DeJong reported that Tridione in dosages of 0.32 gm three times daily was effective in controlling the psychomotor attacks in cases in which the other anticonvulsive drugs had failed

HEADACHE

The observation that distended temporal arteries are sometimes palpable in patients with migraine and that as the attack continues these arteries become more rigid and pipelike and less compressible led Torda and Wolff²⁸ to try to reproduce these findings in cats. The arteries of the ears of 6 cats were studied after infusion for two hours with a solution containing a vasodilator, acetylcholine being used. Measurements demonstrated thickening of the arterial walls of the infused ears. It was also observed that a vasoconstrictor, ergotamine tartrate, was less effective in constricting arteries with thickened walls than in constricting those with normal walls. It was suggested that with prolonged dilatation during attacks of migraine the cranial arteries may undergo similar changes, thus explaining the rigid pipelike texture of the arteries and the decreased ability of ergotamine tartrate to reduce promptly the intensity of the headache.

Friedman, Brenner and Merritt²⁹ injected 0.1 mg of histamine base intravenously in patients subject to recurring attacks of headache and in controls. The headache that usually follows such an injection appeared to be closely dependent on a secondary rise in blood pressure that follows the initial fall, as shown by the absence of such a rise in patients in whom headache failed to develop, the temporary disappearance or amelioration of the headache caused by compression of the carotid artery and the temporary disappearance of the headache following a secondary injection of histamine. Support or the lack of it afforded the walls of the intracranial arteries by the cerebrospinal-fluid pressure seems to play a small part in the production of such headaches, as shown by the absence of improvement during jugular compression or, in most cases, during inhalation of an oxygen and carbon dioxide mixture. The essential mechanism of experimentally produced histamine headache seems to be the mechanical stimulation of pain-sensitive structures in or near the walls of intracranial arteries, caused by distention of the relaxed walls by blood driven in under increasing pressure.

CEREBROVASCULAR LESIONS

In a comprehensive review of vascular disease of the nervous system, Aring³⁰ correlates the various manifestations of cerebrovascular disease with the known facts regarding the physiology of cerebral circulation. He emphasizes the fact that the main factors that control the cerebral circulation are extracerebral. Such occurrences as sudden reduction in systemic blood pressure may be followed by lesions

in a brain that has pre-existing pathologic changes in its vessels. Similarly, changes in the permeability of blood vessels in patients with disease of the cerebral vessels may be followed by a cerebrovascular lesion.

Wolf, Goodell and Wolff³¹ made a follow-up study of patients with subarachnoid hemorrhage. They found that the mortality rate from the first episode of bleeding was 29 per cent. Fourteen per cent of the patients died from recurrence of the bleeding within two to four weeks, and an additional 5 per cent were dead within one year. On the basis of these findings, the authors recommend that an arteriogram be performed on all patients who come under observation during the first four weeks after a subarachnoid hemorrhage. If an aneurysm is visualized, a craniotomy should be performed and the aneurysm treated surgically. Patients who have had their hemorrhage more than four weeks previously and who have localizing signs of an intracranial mass should receive arteriography and craniotomy if suitable indications exist.

THE CENTRAL NERVOUS SYSTEM IN VARIOUS SYSTEMIC DISEASES

Knutson and Baker³² studied in detail the tissues in 12 patients who had died of uremia. They state that these cases may manifest symptoms covering the entire field of neuropsychiatry. Most frequently these are convulsions and coma, but in isolated cases unusual syndromes, such as monoplegia, hemiplegia, aphasia and all varieties of mental symptoms, may be present. There were widespread changes in the nervous system involving both the nerve cells and the parenchymal elements. If the disease ran an acute course, the predominant alteration occurred in the cortical neurons. In the chronic cases, the striking changes were parenchymal rather than neuronal, consisting of focal and perivascular demyelination and necrosis, although neuronal changes were also present.

Ferraro, Arieti and English³³ examined the brains of 5 patients with pernicious anemia in whom the manifestations of this disease appeared to have developed in the course of a psychosis. One case of pernicious anemia without psychosis and 1 that developed a psychotic syndrome in the course of an established pernicious anemia were also reported. The psychosis was of the paranoid schizophrenic type, with ideas of persecution and grandeur, and a withdrawal type of behavior. The pathologic picture, which occurred in all cases including the one without neuropsychiatric symptoms, consisted of vascular changes, — mild endarteritis and proliferation, — ischemic cell changes, clumping of glial cells about vessels and the presence of areas of demyelination that tended to coalesce. In 2 cases the vascular changes typical of Wernicke's encephalopathy were found. These changes were most intense in the regions usually involved in that disease.

Since no mental symptoms were observed in a case that showed the same neuropathologic alterations, the hypothesis is advanced that the organic changes merely precipitate or sensitize one toward a psychosis the type of which is predetermined by psychologic or constitutional mechanisms

Two cases of disseminated lupus erythematosus with neuropsychiatric symptoms are described by Daly.³⁴ These symptoms included toxic delirium, frank psychosis, coma and convulsions. Characteristically, neurologic examination showed scattered motor, reflex and sensory changes that shifted rapidly on repeated examination. Pathologically, the essential damage to the brain consisted of extensive vascular changes similar to those found elsewhere in the body, with a diffuse type of nonspecific encephalitis.

Yannet and Lieberman³⁵ found the incidence of incompatible mother-child Rh blood typings to be significantly higher in a group of undifferentiated mental defectives than in a control group. This suggests that the cerebral abnormality of some of these undifferentiated defectives is probably related to maternal Rh isoimmunization during pregnancy. Of the 19 cases in the undifferentiated group in which this etiologic possibility existed, 6 cases were found in which either definite or presumptive evidence of maternal isoimmunization was present. The neonatal history in all 6 of these cases was considered compatible with the diagnosis of erythroblastosis fetalis. These children showed disorders of muscle tone, choreoathetosis and cerebellar dysfunction.

Two cases of acute idiopathic porphyria are reported by Denny-Brown and Sciarra.³⁶ In the first case, a brief delirium with tremor, associated with passage of burgundy-colored urine, was followed by recovery. In the second, the more usual abdominal cramps, with delirium, convulsions, severe motor paralysis and passage of burgundy-colored urine, occurred in two attacks separated by an interval of two years. The patient died during the second attack, and pathological examination revealed lesions of an ischemic nature in the peripheral nerves. The possibility of the presence of some locally acting vasoconstrictor substance is discussed in relation to the pathogenesis of the visceral disorders of porphyria.

Hoeffler, Guttman and Sands³⁷ report 27 cases of verified adenoma of the islet cells of the pancreas with symptoms of hyperinsulinism that were carefully studied from the psychiatric, neurologic and laboratory points of view. A variety of neuropsychiatric manifestations was found in all patients, usually clearly associated with the fasting state, with the patients usually aware of this relation, some having increased their food intake to the point of becoming obese in an effort to forestall attacks. The clinical data fell into four groups. The most frequent autonomic visceral symptoms, occurring

in 22 patients, were lightheadedness and sweating, headache and less often abdominal pain, nausea, vomiting, pallor, ravenous hunger and coldness. Somatic neurologic abnormalities were observed in 25 patients. Sixteen had motor symptoms, usually consisting of generalized weakness, tremor and incoordination and less often hemiplegia, — 1 patient had a residual hemiparesis, — diminished or absent reflexes and bilateral Babinski signs. The most frequent sensory symptoms were paresthesias, occurring in 15 patients. Fifteen patients had disturbances of vision or of the extraocular motor system, usually in the form of diplopia, blurring of vision or nystagmus. Five patients had transitory aphasia. Psychomotor symptoms occurred in practically all patients. Most frequently seen were confusional states, dullness and noisy behavior, and less frequently there were inability to concentrate and irritability. Phenomena suggestive of fragmentary or full-blown seizures were noted in 22 patients. Deep coma was seen in 15 patients. Nine showed purposeless random movements, thought by some observers to resemble extrapyramidal dyskinesias. Five patients had fainting spells, 5 had actual grand-mal attacks observed on the wards, and 1 patient had sensory Jacksonian episodes without loss of consciousness. Two patients had staring spells suggestive of petit-mal attacks.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32291

PRESENTATION OF CASE

A forty-eight-year-old man entered the hospital because of painless jaundice.

For three weeks before admission the patient was easily fatigued. His weight dropped from 170 to 150 pounds. Three weeks before admission his wife noticed that his skin was yellow, and a physician pointed out that the urine was dark and the stools light. In the last week before admission there was generalized itching of the skin. There had been anorexia for the previous two days, but no nausea, abdominal pain or tenderness, or fever. There had been no previous episodes of jaundice and no history of excessive alcohol consumption.

On physical examination the skin, scleras and mucous membranes were deeply jaundiced. The heart sounds and breath sounds were faint, and the lung fields were hyper-resonant. The neck veins were full in the upright position. The liver edge extended 2 cm. below the costal margin and was not tender. The left border of the prostate felt hard and slightly irregular, but there was no enlargement. There was no edema or ascites. The tongue was normal. The spleen was not palpable.

The temperature was 99.8°F, the pulse 70, and the respirations 20. The blood pressure was 96 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 4,100,000 and 118 gm. of hemoglobin. The white-cell count was 8000, with 60 per cent neutrophils. The urine had a specific gravity of 1.012 and gave a +++ reaction for bile. The

stools, which varied from clay colored to brown, were guaiac negative on five of eight examinations and positive on the others. A chest film and a gastrointestinal series were negative. The serum bilirubin was 29.9 mg. per 100 cc. direct, and 38.0 mg. indirect, the total protein was 6.9 gm., the albumin 4.2 gm. and the globulin 2.7 gm. per 100 cc. A cephalin flocculation test was \pm at twenty-four hours and ++ at forty-eight hours. The total cholesterol was 255 mg. per 100 cc., with 65 per cent cholesterol esters. The phosphorus 2.8 mg., the non-protein nitrogen 19 mg. per 100 cc., and the alkaline phosphatase 9.2 Bodansky units. The prothrombin clotting time was 20 seconds (normal, 19 seconds). Duodenal drainage yielded colorless fluid with a pH of 7.4, the sediment contained innumerable white cells that were not bile stained, and no cholesterol crystals or calcium bilirubinate pigment was seen.

In the hospital the temperature ranged from 99.8°F to normal and subnormal.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED KRANES: This case is fairly typical of a group of cases that to my mind are clinically undiagnosable, usually for quite a long period. The group comprises cases of deep painless jaundice of relatively short duration in which the laboratory findings, physical examination, x-ray films and history are essentially negative. The diagnosis is ultimately made in one of two ways: either by the passage of time during which the patient gets well, or at operation, as in the case under discussion. I am not at all sure that, confronted with a similar problem, I should have had the patient operated on quite so soon. I think that less harm is done by a delay of several weeks than by operating needlessly on a patient with hepatitis. For the problem here is whether this patient had acute hepatitis or obstructive jaundice. Since the advent of vitamin K therapy it is no longer dangerous to postpone surgery for a week or two while the patient is under intensive medical care. On the other hand, it is inadvisable to operate on a patient with acute hepatitis.

The real decision is whether the patient had obstructive jaundice. If he did, the nature of the obstruction is nothing more than a guess. On the whole the evidence favors an obstructive type of jaundice, but I do not believe that one can be certain of that from the evidence at hand.

Reviewing the history and physical examination, one would like to know what this patient's occupation was, to make certain that there were no occupational hazards, so far as liver intoxication is concerned, and whether he was taking any drugs. Presumably neither one of these factors was important in this case, otherwise, it would probably have been mentioned. I am somewhat puzzled about the history. The fact that the patient's weight went from 170 to 150 pounds without any obvious reason is quite puzzling. It is stated that anorexia did not develop until a few days before admission, and yet during the period before admission the patient lost 20 pounds. I am inclined to believe that the disorder of appetite must have been present for a considerable time. One would like to know whether the patient consulted a physician simply because his wife had noticed that the skin was yellow or whether he had symptoms at that time. The statement is made at the beginning that the stools were light colored, and it would help considerably to know whether they remained light colored during that three-week period at home. Later, when he entered the hospital, the stools were not consistently clay colored, so that if any obstruction were present one can assume that it was not constant, since bile pigment was getting through.

The physical examination adds nothing to the picture. The only finding that may need comment is the hard and irregular prostate. It is difficult to believe that that casts any light on the problem, even assuming that the prostate was carcinomatous. I cannot conceive that such a degree of jaundice was caused by metastatic carcinoma of the liver, which rarely produces jaundice, except in the terminal stages, when almost the entire liver is replaced by metastatic tumor tissue.

So far as the laboratory work is concerned, the most important finding was in the stools, which varied from clay colored to brown, indicating that bile was getting through occasionally. The fact that a duodenal drainage done later yielded a colorless fluid simply means that no bile was getting through at that particular time, one must not assume that the obstruction was complete.

I do not know just how to interpret the guaiac-negative and guaiac-positive stools. One naturally assumes that a guaiac-positive stool in the presence of weight loss and intense jaundice signifies some neoplastic lesion in the duodenal region. That is not necessarily true. People with jaundice have guaiac-positive stools. Deeply jaundiced people have a hemorrhagic tendency, although the prothrombin

time in this case was normal. One would like to know how positive the stools were, whether + or ++++. The rest of the laboratory findings except for the van den Bergh reaction are not helpful. One or two straws in the wind point toward an obstructive lesion—the elevated cholesterol and cholesterol ester ratio, and the elevated alkaline phosphatase. Neither one is conclusive, to be sure, but both suggest an obstruction of the biliary tract.

DR TRACY B MALLORY. The guaiac reactions of the stools were + and +++.

DR KRANES. In that case we cannot attach too much significance to the stools. I am still somewhat puzzled and find it difficult to decide whether the jaundice was or was not obstructive. On the whole the evidence is slightly in favor of an obstructive lesion, but I should like to point out that everything recorded could well be found in a case of acute hepatitis. Certainly many patients with severe cases of hepatitis have persistently clay-colored stools. If this patient were twenty-eight years of age instead of forty-eight there would be little doubt about the advisability of waiting to find out what course the disease might take. At the former age acute hepatitis is more frequent than obstructive lesions of the biliary tract. But the patient was forty-eight, and at that age acute hepatitis is less frequent. It does occur, however, and must be kept in mind. At the age of forty-eight, with a history like this, the chances are in favor of an obstructive lesion of the common duct, which is what I believe this patient had, although one cannot be sure.

Having assumed that it was an obstructive lesion, all one can do is guess its nature. There are two main possibilities: obstruction by a stone and neoplastic obstruction of the common duct. We have all encountered cases of gallstone obstruction that were painless, but I should expect some sort of abdominal distress. A complete and totally painless jaundice with stones seems unusual and is unlikely in this case. The betting is somewhat in favor of a neoplastic lesion, probably a carcinoma of the common bile duct or of the ampulla, or a carcinoma of the head of the pancreas. Certainly the weight loss, the clay-colored stools, the elevated cholesterol and cholesterol esters and the positive guaiac tests on the stool make such a diagnosis at this age more attractive than any other diagnosis. Although I still do not know what this man had, the most probable lesion is a carcinoma of the ampulla or bile duct, an obstructive lesion, but it would not surprise me if it turned out to be acute hepatitis.

DR ROBERT S PALMER. Would Dr Kranes consider doing a liver punch biopsy?

DR KRANES. I think that a peritoneoscopy and biopsy of the liver before actual surgery would be a logical procedure rather than waiting too long.

DR MALLORY. A peritoneoscopy was done.

DR. EDWARD B. BENEDICT No lesion was grossly visible in the liver, but we took a biopsy that gave us the answer

DR. MALLORY Unfortunately the biopsy did not exactly give us the answer

DR. BENEDICT At least it gave us a pathological report

CLINICAL DIAGNOSIS

Carcinoma of head of pancreas?

Carcinoma of ampulla of Vater?

Infectious hepatitis?

DR. KRANES'S DIAGNOSIS

Carcinoma of common duct? -

Acute hepatitis?

ANATOMICAL DIAGNOSIS

Infectious hepatitis

PATHOLOGICAL DISCUSSION

DR. MALLORY The biopsy was done during a period when I was absent from the city. The clinicians were impatient for an immediate diagnosis and were content with an oral report from one of the junior men, who believed the lesion to be consistent with obstructive jaundice. Without further delay an exploratory laparotomy was done. No evidence of obstruction was found, and another biopsy of the liver was done. Following operation the patient's jaundice temporarily increased, after which he began a slow but apparently complete recovery and left the hospital entirely well.

When I returned and was shown the first biopsy specimen I considered it reasonably typical of infectious hepatitis. It showed periportal inflammatory infiltration of mononuclear cells, foci of intralobular inflammation and acidophilic necrosis of individual liver cells. In the second specimen the process had cleared to a considerable degree, and the diagnosis was more difficult. I have had the advantage of seeing a large number of biopsies of cases of epidemic hepatitis during my experience in the Army. Before this experience I have no confidence that I should have recognized the lesion. Most pathologists expect to find extensive central necrosis, such as is seen at autopsy in fatal cases. In nonfatal cases this necrosis is rarely found.

DR. BENEDICT How do you explain the marked weight loss and absence of fever?

DR. MALLORY Fever is a variable symptom and is most frequently seen in the prodromal period before jaundice. I cannot explain the weight loss.

DR. KRANES I should like to ask the surgical point of view on how long to wait when it is difficult to decide. What harm comes to these patients under careful observation?

DR. FIORINDO A. SIMEONE The longer one allows the obstruction to continue, the greater the chance of irreparable harm to the liver cells and the more difficult it is to correct a disturbance such as the prothrombin formation.

DR. CLAUDE E. WELCH There is an additional consideration if this had been a carcinoma of the ampulla, it might have passed the curable stage during the period of observation.

DR. KRANES How long would that be? It is difficult to believe, since the patient had been jaundiced for three weeks, that two weeks' observation would make such a difference.

DR. WELCH I should hesitate to wait longer than two weeks. It is a difficult decision to make.

CASE 32292

PRESENTATION OF CASE

A twenty-five-year-old man, a window decorator, entered the hospital because of dizziness, double vision, headache, nausea and vomiting.

The patient had always been in good health except for occasional "sinus trouble," which was never severe enough to cause him to consult a physician. Five years before admission the patient was discharged from the Army because of bilateral otosclerosis and deafness. Six weeks before entry he noted the sudden onset of dizziness while decorating a window. Things seemed to dance up and down in front of his eyes. A physician found "low blood pressure." Five weeks before entry, the patient became aware of diplopia when looking to the extreme right or left. A week later he rapidly developed a severe dull, nonthrobbing, frontal headache. These symptoms persisted, and three weeks before entry he became nauseated and vomited several times. Associated with the dizziness was some stumbling and clumsiness of gait. A week before entry he became drowsy and had difficulty in remembering where he put things. He experienced some chilly sensations but never had a frank chill. Vision was blurred. Four days before entry the nausea had progressed to such an extent that he ate nothing and drank very little. Two days later he was forced to stop work and slept most of the time. He was finally brought by ambulance to the Emergency Ward.

Physical examination revealed a drowsy, slightly obese young man who yawned frequently. Speech was slow but distinct, and he gave an adequate history. The cranium, chest, heart and abdomen were normal. On confrontation the visual fields were normal. The pupils were equal (4 mm) and did not react to light but did react to near vision, although there was absence of convergence. No spontaneous nystagmus was present, but there was nystagmus retractorius of the left eye. Conjugate upward gaze was paralyzed, and downward gaze was weak, lateral conjugate gaze was present to a limited degree. For days all eye movements became progressively weaker and eventually paralyzed. The nystagmus retractorius disappeared, but there was vertical nystagmus on attempted downward gaze. Attempted lateral gaze result-

ed in a slight convergent movement of the left eye. There was no optokinetic nystagmus.

The fundi were normal on admission, but in a week, papilledema (1 or 2 diopters) was present, in addition to a small flame-shaped retinal hemorrhage on the left side that was followed in a few days by a similar hemorrhage on the right. Hearing was markedly impaired bilaterally. The neck was quite stiff. The fifth, seventh, tenth, eleventh and twelfth nerves were normal. There was some unsteadiness in performing the finger-to-nose test on the right, and the Kernig test was positive. The arm and knee jerks were difficult to elicit and were bilaterally equal. The ankle jerks were ++ and equal. There was a flexor-plantar reflex bilaterally.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 60 diastolic.

Examination of the blood revealed a red-cell count of 5,360,000, with 110 per cent hemoglobin, and a white-cell count of 9040, with 76 per cent neutrophils. The nonprotein nitrogen, chlorides, carbon dioxide and fasting blood sugar were normal. Repeated blood cultures were negative. The blood Hinton test was negative. Lumbar puncture yielded an initial pressure equivalent to 215 mm of water and a final pressure equivalent to 130 mm. The spinal fluid was questionably xanthochromic and contained 6 red cells, 45 lymphocytes and 6 polymorphonuclears per cubic millimeter. The protein was 98 mg, the sugar 11 mg and the chlorides 680 mg per 100 cc. The urine had a specific gravity of 1.022 and was normal except for a ++ test for acetone. There was no albumin or sugar. Smear and culture of a pellicle formed on standing were negative for tubercle bacilli. A guinea pig was inoculated. A tryptophane test on the spinal fluid was positive.

A tuberculin skin test was negative in a dilution of 1:1000. X-ray films of the chest and skull were negative. The pineal body was not visualized.

The patient continued to be drowsy but could be aroused. On the third hospital day the temperature suddenly rose to 105°F, and he became stuporous and incontinent. No reflexes could be obtained. The plantar reflexes were flexor bilaterally. He was given alcohol sponges and penicillin. At no time did he receive sulfonamides. The temperature continued to climb, reaching a peak of 107°F on the fourth hospital day. On the sixth day it was down to 99°F, but rose again to 104° in the evening and gradually dropped to 99°, running a moderate spiking course. The state of consciousness approximately paralleled the temperature, but the patient never regained full consciousness. On repeated lumbar punctures the spinal-fluid pressure was equivalent to 230 to 300 mm of water. The fluid was xanthochromic, with 20 to 25 white cells per cubic millimeter, of which a few (1 to 6) were polymorphonuclears. The total protein remained elevated

(56 to 98 mg per 100 cc). The sugar rose to 65 and 89 mg per 100 cc (punctures performed following infusions of 5 per cent dextrose in saline), and the chlorides rose to .827 milliequiv per liter. The gold-sol curve was 0001121100. Dynamics, performed on the fourth lumbar puncture, were normal.

On the twelfth hospital day a red petechial eruption, which blanched on pressure, appeared over the back, dependent regions of the shoulders and upper arms, gradually spreading over the entire body and assuming a maculopapular character. On the following day the nonprotein nitrogen was 205 mg per 100 cc. The patient was totally incontinent, passing many diarrheal stools that were negative for pus, parasites and occult blood. On the fifteenth hospital day the nonprotein nitrogen had risen to 260 mg per 100 cc. The carbon dioxide was 12.1 milliequiv and the chlorides 104 milliequiv per liter. An indwelling catheter was placed, and although oliguria had been suspected the measured output rose to approximately the intake. The specific gravity was 1.010 on repeated examinations, and a ++ test for albumin was found. Abundant colon bacilli were grown in urine culture. Repeated chemical determinations showed continued high nonprotein nitrogen, reaching 290 mg per 100 cc on the twentieth hospital day. The carbon dioxide content, however, gradually rose to 20.9 milliequiv per liter. On the sixteenth hospital day an x-ray film of the chest revealed a definite increase in density in the left-lower-lung field. Moist rales became audible at the left base, and the patient developed chills and rapid, shallow respiration. His condition grew rapidly worse, and he died on the twenty-fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR MANDEL COHEN This man was apparently well until the onset of the present illness and over a period of six weeks developed, successively and rapidly, dizziness, slight diplopia, nausea, vomiting, stumbling and drowsiness. He was taken to the hospital, where it was found that he had some signs indicating that the midbrain and the cerebellum were involved. A few cells were found in the spinal fluid, and there was fever. The question no doubt came up whether the disorder was infection or neoplasm. He became worse and, after being in the hospital for twelve days, developed nitrogen retention and a rash. Nitrogen retention progressed, and death followed.

From these data it is not possible to determine exactly the nature of this disorder. There were, however, signs and symptoms that point fairly definitely to the location and that give a lead regarding the possible causes of the lesion. To begin with, the symptoms of dizziness, diplopia, nausea, vomiting, stumbling and drowsiness could be related to disease involving the cerebellum or cerebellar connections. The neurologic examination showed

predominantly difficulties with eye movements that were not paralysis of isolated nerves but concerned conjugate movement, upward movement, downward movement and lateral movement, in addition, the pupils measured 4 mm and did not react to light, but did react during accommodation. Convergence of the eyes was absent. All that taken together means that the midbrain was involved. Was it involved by a mass in the midbrain, or was it involved by something pressing on the midbrain? I cannot tell the difference. Incidentally the patient had nystagmus retractorius. After a certain amount of investigation and aid from Dr. Cogan, I discovered the meaning of this term. When co-ordination of eye movements is poor all the muscles may move together. An attempted eye movement results in eye retraction, this is supposed to be due to distribution of connections of the nuclei of the third nerve. All these eye signs point definitely to disorder affecting the midbrain. One might ask why we did not think that the nerves individually were involved. The patient did not have obvious strabismus, it was not possible to demonstrate isolated paralysis of nerves, and the eyes followed objects. Midbrain localization was therefore indicated. It is probable that the lesion or lesions were in the neighborhood of the midbrain and the anterior part of the cerebellum.

The next question to decide is the nature of the disorder. Because of the progressive course, this disorder probably was not a thrombosis of the blood vessel or vascular disease, because of the evidence of increased intracranial pressure and the lack of other typical signs, it was probably not any of the so-called "degenerative diseases," such as acute encephalomyelitis and multiple sclerosis. That leaves the problem of what could cause increased intracranial pressure and develop rapidly within about six weeks, with death following soon thereafter. It seems to me that one cannot tell absolutely whether this was a tumor or an infectious disorder. The course of the illness, which was rather brief for that of tumor, suggests some infectious disorder. Neoplasm involving the area of the midbrain, however, often runs a rapid course. In Dandy's¹ series some tumors of the third ventricle ran half a year's course between the first symptom and operation. The short course is therefore not diagnostic, except that it is somewhat short for a tumor.

In considering infectious disorder of the brain, one must include an infectious mass—that is, abscess or tuberculoma. One would then like to have some idea of what such a mass is secondary to, because by and large, if a patient has brain abscess or tuberculoma, there is some evidence of primary infectious disease. There was no evidence of tuberculosis in the lungs or elsewhere or of a focus of infection suggesting a brain abscess. Five years before admission the patient was discharged from the Army because of bilateral otosclerosis and deaf-

ness. I wonder whether he had bilateral otitis media all the time, but I assume that the ears were examined in this hospital and were normal. Apparently this patient's "sinus trouble" was never severe enough for him to consult a physician. That type of history is of no help in an attempt to find the focus of infection for brain abscess. Usually clear-cut evidence of otitis media, sinusitis or lung disease is found, but this patient did not have such evidence. That is a serious drawback to the diagnosis of infection, such as abscess.

Does the fever help in the differential diagnosis? By and large, it is safe to assume that if the patient had fever he had infection. One serious exception, however, is when a patient has disease around the midbrain and hypothalamus, which I suppose is exactly where the disease occurred in this patient. There are well authenticated cases of continuous fever from lesions in that region. In general, most diagnoses of neurogenic fever and probably all so-called "psychogenic fever" lead to the wrong answer. Consequently even fever does not help in the decision between tumor and infection.

Does the spinal fluid help in the differential diagnosis? The few cells make one think not of obvious meningitis but of a mass like abscess or tuberculoma that is irritating but does not actually infect the ventricular and subarachnoid spaces. Tumors, particularly those involving the third ventricle or other ventricles, also give a few cells and even a few polymorphonuclears. What about the spinal-fluid sugar? In general, a low spinal-fluid sugar means the active presence of bacteria, tubercle bacilli or yeast. The first sugar determination was quite low (11 mg per 100 cc), and subsequent tests were within normal limits. One possibility is that the first sugar determination was wrong—that the fluid stood for a day or two before analysis.

DR. JAMES MEATH: The first sugar determination was done on the day following lumbar puncture.

DR. COHEN: The lumbar puncture was done, and the fluid stood over night and was analyzed later. Falsely low sugars can be obtained under such circumstances. That is quite possible in this case because the cells were not high enough to go with such a low sugar. The blood sugar level affects the spinal-fluid sugar with a high blood sugar after a clysis or intravenous injection the spinal-fluid sugar may be falsely high. In bacterial infection it is also possible for patients being treated with penicillin to have bacteria in the spinal fluid, the sugar remaining high in the presence of penicillin. Apparently under these conditions bacteria are not able to use sugar. All one can say is that the patient had one quite low sugar and two normal ones. In tuberculous meningitis, if the sugar is once low, it is apt to remain low. The cultures, I gather, were all normal. Were cultures taken of the spinal fluid when the patient was not getting penicillin?

DR. MEATH: Yes.

DR COHEN Final conclusions cannot be drawn from a good part of the data. One must say that the course could be tumor or infection, and the spinal fluid could go with either. There was no good source for infection.

We are left with the possibility of a mass that was in the cerebellum, pressing on the midbrain or, less likely, in the midbrain itself and was either neoplastic or infectious in origin. If infectious, the mass was probably tuberculoma or something of that sort rather than an abscess.

The neurologic disorder progressed, and on the twelfth day a petechial eruption of a maculopapular character developed, from that point on nitrogen retention was noted. The nonprotein nitrogen rose steadily, and there were acidosis and diarrhea. All we are told about renal studies is that cultures gave abundant colon bacilli. The patient presumably did not have pus in the urine. Is that right?

DR TRACY B MALLORY When he first came in he had a specific gravity running from 1.020 to 1.030, with no albumin and only one or two white cells per high-power field on smear. Terminally, after he had an indwelling catheter for many days, there was pus in the urine.

DR COHEN The patient then developed what seemed to be pneumonia and died. How can one relate this development of uremia with the intracranial disease? One can speculate about various syndromes associated with brain and renal disease, but none of them seem clinically applicable in this case. Could there have been hypertension or vascular disease of a malignant type, which led to brain lesions and then to renal failure? This case does not give the picture of that syndrome, either by course or by signs. Another possibility is a renal tumor that metastasized to the brain and later showed itself as renal disease; again, there is no evidence whatsoever. Other conditions such as periarteritis nodosa which involve the brain and kidney, can be mentioned, but there is no evidence.

Were any drugs besides penicillin given?

DR MALLORY No.

DR COHEN Does penicillin, like the sulfonamides, cause uremia? The only evidence is that nitrogen retention occasionally occurs during the administration of penicillin, but for all practical purposes a renal complication is not attributable to penicillin.

Could this patient have had a bacterial infection, septicemia, brain infection and, terminally, renal infection? Again, there is no evidence. I gather that there was no retrograde pyelogram or anything like that, which might have helped somewhat.

Could tuberculosis of the kidney have been associated with the alleged tuberculoma of the brain? That is not likely, the uremia would not be consistent with the brain disease. Perhaps cystitis and pyelonephritis developed terminally. That is not a satisfactory explanation, but I do not see any other, in the absence of drugs such as sulfanilamide.

In conclusion, this man had a disease that came on fairly rapidly and seemed to involve the region of the cerebellum and the midbrain, causing increased intracranial pressure, fever and cells in the spinal fluid. Further information in such a situation could be obtained from injections of air into the ventricles. I suppose that procedure was done. There was a mass, in all likelihood in the neighborhood of the cerebellum and the inferior cerebellum peduncle or, possibly, in the midbrain, it could have been a pinealoma that was pressing on the brain stem. I cannot go any farther from the evidence.

Since I must make a definite diagnosis, I believe that the patient had a brain tumor, and my second choice is tuberculoma.

DR MALLORY There are two very definite phases to this case, the cerebral and the renal. Dr Dahl, will you give the impression on the wards?

DR LEWIS K DAHL Dr Burnett actually followed the case. None of us suspected what was really found. I think that the most prevalent opinion on the wards was that this was periarteritis nodosa, because of the hypertension and the renal and cerebral signs.

DR JAMES B AYER Is the record here? May we see the temperature chart?

DR MALLORY The printed record does not give any idea of the extreme elevation of temperature. On the ninth hospital day the temperature was normal, on the tenth it was 105°F, and on the morning of the eleventh it was 107°F, despite practically constant alcoholic sponges, ice packs and so forth, dropping on the following day back to 99°F — a severe and prolonged hyperthermia.

DR WYMAN RICHARDSON May we see the x-ray film of the chest?

DR JAMES R LINGLEY This film, taken with a portable apparatus, shows a great deal of motion. There is a small area of density, however, at the left base consistent with consolidation. This film was taken just before death.

CLINICAL DIAGNOSES

Tuberculous meningitis?
Periarteritis nodosa?
Subacute bacterial endocarditis?
Brain tumor (pinealoma-lesion in midbrain)?
Toxic nephritis

DR. COHEN'S DIAGNOSIS

Brain tumor (? pinealoma)
Tuberculoma?

ANATOMICAL DIAGNOSIS

Pinealoma

PATHOLOGICAL DISCUSSION

DR MALLORY I shall discuss the renal situation first and let Dr Kubik tell us what was found in the central nervous system.

The kidneys showed a lesion that has become familiar during and since the war. There was a frank

hemoglobinuric nephrosis, with degeneration in the lower segments of the nephrons, a considerable amount of interstitial nephritis and precipitation of hemoglobin pigment in the tubules. The kidney was of the type seen with mismatched transfusion, crush syndrome, blackwater fever, burns and a number of other situations. A fairly frequent cause of such a renal injury is sulfonamide sensitivity. This man, we know, had received no sulfonamides. In the kidneys there were some questionable crystals, but on analysis in the chemistry laboratory no sulfonamides were found. The sulfonamides can therefore be completely ruled out. There had been no transfusion, no plasma and no obvious cause of hemolysis.

At the United States Army Institute of Pathology in Washington there were 120 fatal cases of heat stroke. In that group, 10 or 15 patients developed severe hemoglobinuric nephrosis and died in uremia several days after recovery from the heat stroke. In some of those cases, despite a clinical state of shock, neither whole blood nor plasma was used in treatment. Nevertheless the patients showed massive precipitation of hemoglobin in the kidneys. That is the only explanation one can find for this case. The hyperthermia was so marked that the same physiologic mechanism seen in heat stroke might easily have been involved.

DR. CHARLES L. SHORT: In artificial-fever therapy patients have been subjected to temperatures of 106.7°F for eight hours in this hospital and in Rochester, New York, by Dr. Stafford L. Warren for thirty hours, but I remember that no cases of this syndrome were found. The patients were in reasonably good physical condition.

DR. MALLORY: The lesion is one that has been generally recognized by pathologists only within the last few years, so that I hesitate to accept a case reported over five years ago. It was probably not the hyperthermia but the subsequent shock that was responsible.

DR. CHARLES S. KUBIK: This was a tumor of the pineal region, which, I have been told, was the diagnosis made on admission by one of the house staff, who based his opinion on the defective upward conjugate movement of the eyes. This, as Dr. Cogan said in discussing another case,² is practically always a dependable sign of a lesion involving the quadrigeminal bodies and, in my experience, has occurred most frequently through, although not exclusively with, pinealomas and tumors in the pineal region. In this case subsequent findings and developments made the diagnosis more difficult.

On sagittal section of normal brain showing the relations of the pineal body, which is situated in the midline immediately above the superior quadrigeminal bodies and at the posterior extremity of the third ventricle just above the anterior end of the aqueduct, the pineal recess of the third ventricle actually dips into the pineal body. The spinal fluid is formed in the lateral ventricles, passes through the foramen of Monro into the third ventricle, and

thence through the aqueduct into the fourth ventricle from which it enters the subarachnoid space through the foramina of Magendie and Luschka. It is readily seen why tumors in the pineal region lead to internal hydrocephalus by obstruction of the aqueduct.

In the brain in the case under discussion, behind the optic chiasm, there was a rounded prominence 1.3 cm. in diameter, which represented the floor of the third ventricle; it bulged downward because of dilatation and was also invaded by tumor. Horizontal sections of the brain showed the tumor, measuring 2.5 to 3 cm. in diameter, in the pineal region. It extended forward in the third ventricle between the optic thalami, which it invaded. It also extended downward, invading the tegmen of the midbrain and completely filling the aqueduct and the upper part of the fourth ventricle.

Anterior to the main tumor mass, the ependyma of the third ventricle and of the anterior horns of the lateral ventricles was covered with tumor implants. Implants in the third ventricle in these cases are fairly frequent and sometimes, through involvement of the hypothalamus, lead to diabetes insipidus, even when there are no clinical indications of tumor in the pineal region. There was no diabetes insipidus in this case, but the tumor involvement of the hypothalamus probably accounted for the fever.

Of the several pinealomas examined, all invaded the midbrain, none could have been removed by operation.

Histologically the tumor in this case was composed of rather large, rounded and fusiform cells with well defined cytoplasm and also of cells with poorly defined cytoplasm. An unusual feature was the presence of multinucleated cells and many giant cells, some of which had as many as twenty visible nuclei. I believe that these were tumor cells and not foreign-body giant cells.

The histologic findings were somewhat different from those observed in other cases of pinealoma, which are usually composed of fairly large rounded and polyhedral cells and are frequently infiltrated with lymphocytes and sometimes with lymphocytes and plasma cells. In the case recently discussed by Dr. Cogan² the tumor cells resembled very closely the cells of the normal pineal body, and there was little or no infiltration with lymphocytes.

In this case the fusiform and giant cells were unusual, but the gross findings were similar to those of pinealoma, indicating that the tumor began in the pineal region and later invaded the midbrain and optic thalami. Fusiform and giant cells are frequent in some of the gliomas, and since the parenchymal cells of the pineal body are derived from glial cells I suppose that similar de-differentiation occurs in a pinealoma.

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"LETHEON"

THE present year is one that merits more than ordinary consideration in the history of surgery and in the annals of the Massachusetts General Hospital, for it was one hundred years ago this fall, in the surgical amphitheater then under the hospital's glass-topped dome, that painless surgery was given its first public demonstration, and a new surgical era began. In 1921, with fitting ceremonies, the hospital observed its own one hundredth anniversary, on October 16, 1946, it will celebrate the centenary of its greatest single service to humanity.

The properties of sulfuric ether were far from unknown when William Thomas Green Morton, the Boston dentist, administered that volatile sub-

stance, sometime known as "Letheon," to Gilbert Abbott in order that John Collins Warren might painlessly remove a tumor from under the jaw. In the late eighteenth century there is an account of its use in a case of "pectoral catarrh," when two teaspoonfuls were volatilized and inhaled with considerable benefit to the sufferer, its employment was again reported, about the turn of the century, "for the relief of a very painful inflammatory affection of the mamma." We may further read, in Pereira's *Materia Medica*, published in London in 1839, that "the vapor of ether is inhaled in spasmodic asthma, chronic catarrh, and dyspnoea, hooping cough, and to relieve the effects caused by the accidental inhalation of chlorine gas."

We have Dr. Charles T. Jackson's own word for it, in a statement issued in 1847, that he had experimented with ether in 1841, and it is generally recognized that Dr. Crawford W. Long, a physician of Georgia, had used ether as a surgical anesthetic as early as 1842, although he made no public announcement of his experiences until 1849.

Sulfuric ether was not the only volatile substance whose anesthetic properties were the subject of early experimentation. Sir Humphry Davy, the noted English chemist and physicist, had investigated nitrous oxide in 1799 and suggested the use of this gas in surgical operations "attended with little effusion of blood." Horace Wells, a dentist of Hartford, formerly associated with Morton, had later experimented with the gas and had given an unsuccessful demonstration of its use in 1844. The year after ether made its debut Sir James Y. Simpson, of Edinburgh, introduced chloroform as a general anesthetic.

The recognition of anesthesia as the great turning point in surgery took place in the Massachusetts General Hospital. Its official announcement to the medical profession was made through the medium of the *Boston Medical and Surgical Journal*, on November 18, 1846, in the article "Insensibility during Surgical Operations Produced by Inhalation" by Henry Jacob Bigelow, one of the surgeons of the Massachusetts General Hospital. The *Journal* had more on the same subject in the following months, and the hospital report of 1848 announced a total of one hundred and thirty-two

operations performed within its walls using ether as an anesthetic

The ignominious controversy that raged for a time over the credit for the ether discovery takes away nothing from the importance of the event itself. Morton wanted credit and gold, and Dr Charles T Jackson, whose student in chemistry he had once been, put in his claim for a major share of the honor of the discovery. The anesthetic was patented jointly by Morton and Jackson on condition of the latter that he receive one tenth of the profits, and the Board of Trustees of the hospital presented a purse of \$1000 to Morton in 1848. It is not the way things are done today, and Bowditch* no doubt wrote earnestly in his history of the hospital, first published in 1851, that "the patience of the public has been long since thoroughly wearied out by the ether controversy."

The fact remains that through a long one hundred years we have had the blessing of painless surgery, with the refinements that the years have brought to it. We have had the accumulated benefit to those countless surgical patients who have found in anesthesia something like the music of the Lotos-Eaters, to wax poetical

Music that gentlier on the spirit lies,
Than tired eyelids upon tired eyes,
Music that brings sweet sleep down from the
blissful skies

*Bowditch, N. I. *A History of the Massachusetts General Hospital (to August 5, 1851)*. Second edition. With a continuation to 1872 by the Reverend George E. Ellis. 34 pp. Boston: printed by the Trustees from the Bowditch Fund, 1872.

DISABILITY FOLLOWING ACUTE HEPATITIS

THE persistence of liver damage after apparent recovery from acute infectious (epidemic) hepatitis or so-called "catarrhal jaundice," has recently received a certain amount of attention.

Salmon and Richman¹ reviewed some of the recent literature on the subject and reported follow-up studies on 16 characteristic cases. They found liver damage demonstrable by the cephalin-cholesterol flocculation test and by a lowering of the diastatic activity of the serum, which persisted for a period varying from a few weeks to several months after apparent recovery from the acute attack. Others

have demonstrated impairment of liver function by various tests in from 25 to over 60 per cent of patients for periods varying up to several years.

Caravati² noted a clinical syndrome in a number of enlisted men and officers as a sequel to homologous serum hepatitis that followed vaccination against yellow fever. The subjective symptoms of this syndrome were chronic fatigue, discomfort (a mild but constant aching) in the right upper quadrant of the abdomen, digestive disturbances (flatulent dyspepsia) especially after the ingestion of fats, malnutrition and failure to gain weight even on a high-calorie, high-vitamin diet and emotional instability. Studies of these patients revealed no hypoproteinemia, hypocalcemia or anemia, and there was no evidence of vitamin deficiency of any type. Gastric secretion and motility were found to be normal, although some showed a slight degree of hypermotility of the small intestine that was not enough to be considered significant. Studies of pancreatic function in several cases revealed no abnormality. The liver was found to be normal in size, shape and contour, and only a single patient showed evidence of liver disease, as indicated by spider angiomas over the trunk. Various liver-function tests showed no convincing evidence of residual hepatitis or of biliary-tract disease. Caravati believes that this clinical pattern is a constant finding only in such cases and that it does not follow other types of infectious hepatitis. He considers the syndrome to be an alteration of physiology caused by a mild infectious process and by an unfavorable psychic reaction to confinement by long illness. He does think, however, that the liver is probably the source of the physiologic disturbance.

Benjamin and Hoyt³ made a study of 200 soldiers who were returned to the Lovell General Hospital because they had failed to achieve satisfactory convalescence after an attack of jaundice following yellow-fever vaccination. These cases represented only a small proportion of those who originally suffered from postvaccinal hepatitis. They had been in overseas hospitals for several months, and some of them still appeared definitely ill when they arrived, in spite of the fact that five to nine months had elapsed since their original attack of jaundice. As a group these patients were described as "pale,

thin, exhausted and utterly devoid of animation, their reactions, mental and physical, were slow and indifferent." They had had no military training whatsoever since their original illness. Their complaints were extreme weakness, overpowering fatigue, indigestion (particularly for fatty foods), anorexia, pain (especially in the right upper quadrant), nausea and vomiting, backache, insomnia,

nervous irritability and tremors, and anxiety and apprehension (fear of recurrence of jaundice).

From the study of these patients, Benjamin and Hoyt concluded that psychoneurotic patterns may develop as a complication of postvaccinal hepatitis or that antecedent patterns may be reborn. The bromsulfalein test for liver function showed retention of the dye in 32 per cent after twenty minutes and

in 11 per cent after thirty minutes. None of the other patients had objective evidence of liver dysfunction. Improvement in damaged liver functions was still apparent at the end of six months to a year. There did not seem to be any correlation between the laboratory tests and the incidence of palpable liver edges. In 37 patients there was a vasomotor disorder, manifested by pronounced tremor, cold, red, dripping hands and overpowering weakness.

In the course of a study of acute infectious (epidemic) hepatitis in the Mediterranean Theater, Barker, Capps and Allen⁴ observed that certain patients failed to recover promptly and for prolonged periods exhibited symptoms and findings that indicated persistent hepatic disease, with a tendency toward exacerbations and remissions. These cases presented a sufficiently distinctive and uniform clinical picture to justify their consideration as a separate group or syndrome, which they called "chronic hepatitis." In the 76 cases that they studied, the most characteristic and diagnostic feature was the increase in abnormal physical find-

ings, symptoms and laboratory evidence of liver dysfunction produced by exercise. Frequently a patient appeared to have recovered while on minimal exercise, but an increase in physical activity promptly caused the clinical syndrome to reappear. They considered that the essential treatment was adequate bed rest and a high-protein diet. They made an important distinction between active and

inactive hepatitis. The latter group includes patients with objective liver disease but a normal reaction to exercise. In such a situation the symptoms are not disabling, and they believe that no treatment is necessary.

In a paper recently presented at the Harvard Medical Society, Jersild described a number of cases of subacute or chronic hepatitis that occurred in Denmark

during 1944-1945, when there was a widespread epidemic of infectious hepatitis similar to those that occurred in other European countries. In some of the Danish cases the disease started in the usual manner and progressed continuously, whereas in others there was definite temporary improvement, after which the disease relapsed and then progressed. The condition was associated with a high fatality rate and usually occurred in women over forty years of age. Polack⁵ in 1938 described a similar but less severe condition in young adults in Copenhagen after mild attacks of infectious hepatitis.

From all these observations it appears that, although, on the whole, infectious hepatitis and homologous serum jaundice are relatively mild diseases and are associated with an extremely low mortality rate (about 0.2 per cent), cases do occur in which there is a long disabling illness with a variety of symptoms referable to the liver or nervous system or both. It also seems likely that in some of the cases of chronic hepatitis, such as those recently observed in Denmark, and in some of the cases of

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homologous serum jaundice the infectious agent is one that gives rise to persistent and diffuse residual damage or to a progressive hepatic lesion oftener than does the etiologic agent associated with the usual case of infectious hepatitis or catarrhal jaundice. The implications for treatment are obvious. Patients with residual liver damage require particularly long periods of intensive dietary therapy, with avoidance of exercise beyond their tolerances.

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MASSACHUSETTS MEDICAL SOCIETY

SUBCOMMITTEE ON VETERANS' AFFAIRS, POSTWAR PLANNING COMMITTEE

In March, 1946, the Subcommittee on Veterans' Affairs was appointed as a part of the Postwar Planning Committee of the Massachusetts Medical Society. This is in accordance with the sound administrative policy that limits the number of standing or special committees and provides for subcommittees of general committees for specific problems. The subcommittee, composed of five physician-veterans of World War II has met frequently, both independently and in connection with meetings of the Postwar Planning Committee.

The members of the subcommittee were pleased to find that for the past two years or more the Massachusetts Medical Society, through its officers and committees, has attempted to find solutions for the various problems that it was anticipated doctors might encounter on return from service to civilian practice. Foremost of these was judged to be that of postgraduate education and training. In addition to setting up courses of lectures and clinical demonstrations in the seven districts into which the state was divided, the committee arranged for the course of lectures held from February to May, 1946, in Sanders Theater, Cambridge. The latter course proved highly successful, with attendances at the lectures ranging from 400 to 800 physicians. Of these approximately 35 per cent were veterans, a ratio lower than had been anticipated. The second major achievement of the Postwar Planning Committee was the development of the Bureau of Clinical Information at the Headquarters of the Society, designed to serve as a clearing house for

information regarding clinical lectures, ward rounds, operations and so forth that are held daily at hospitals in the Boston area. The bureau has published monthly a mimeographed schedule giving such data in detail for the convenience of veterans and other visiting physicians. The service has been used widely and has received much favorable comment. An unlooked-for development was the demand for a counseling service, which the bureau has supplied so far as its facilities have permitted. Attention should also be directed to the Loan Fund, which is available to all veterans who need it.

From the time of its organization, the Subcommittee on Veterans' Affairs has attempted to find out what other problems were of most concern to returning doctors and has tried to find solutions for such of these as were capable of solution by Society action. Information has been gained from personal interviews, from informal discussions and from questionnaires distributed at the meetings at Sanders Theater and at the annual meeting of the Society. In addition to the all-important matter of postgraduate training, including refresher courses of varying length, residencies and assistant residencies and so forth, the most frequent problems have appeared to be suitable locations for men starting out in practice or changing place of practice from that prior to military service, availability of assistantships for men starting out in practice, hospital-staff appointments, to provide some place for hospitalization of private patients, office space and homes, telephone listings, and rebuilding of practice.

To provide readily available and up-to-date information regarding locations for practice, assistantships, opportunities in industry and so forth the subcommittee has recommended that the Bureau of Clinical Information be expanded and made a permanent installation of the Society, with sufficient personnel, both professional and secretarial, and sufficient space and funds to render this valuable service not only now but in the years to come. This has been agreed to in principle for the coming year by the appropriate authorities. Although most veteran doctors now out of the service have become settled or soon will be, it is believed that the demand for information of the sort outlined will always be great and that it is a natural function of the Massachusetts Medical Society to furnish such, even though it involves considerable expense. There are still in the service thousands of doctors, some of whom will not return to civilian life for two years or more.

The problem of hospital-staff appointments is far from easy. Hospitals in Massachusetts, in common with those all over the country, are filled to capacity constantly and have long waiting lists of patients. Doctors already on the staff have great difficulty in getting their patients in, even when the need for hospitalization is urgent. Nevertheless, the sub-

committee believes that every effort should be made by hospitals to grant staff appointments, even though of temporary nature or on the courtesy staff, to qualified doctors so that the profession will not be in the position of penalizing men for having spent from two to five years in the services. Already the president of the Massachusetts Hospital Association has sent communications to all hospitals of the Commonwealth urging that particular consideration be given to qualified veteran doctors applying for staff appointments. This supplements similar letters sent long before V-J Day by the Postwar Planning Committee to hospital superintendents, chiefs-of-staff and presidents of boards of trustees of all Massachusetts hospitals. It is earnestly hoped that all hospitals will co-operate in this important matter.

The matter of office space and homes, although acute everywhere, has not appeared to be insurmountable. It is a local problem that has almost invariably yielded to industrious search on the part of the returning veteran. Often he has not been able to secure exactly the type of office and home that he desires, but he has been able to get some type of satisfactory arrangement. The subcommittee urges that each physician having ample office space share it with a returning doctor until such time as the veteran is able to find an office for himself.

Because of the shortage of paper, telephone directories cannot be printed so often as in prewar days, consequently, some physicians will have to wait for some months before being listed. In conferences with the subcommittee, representatives of the telephone company have been most sympathetic and co-operative. The problem, however, is large and involves not only doctors but also other professional and business groups. The best solution at the moment is that returning doctors, when established, take steps to inform their patients of their new address and telephone number. The telephone company has increased its information service and states that within twenty-four hours of the installation of a telephone, the number can be secured through such service. Detailed information on this point was published in the April 18, 1946, issue of the *New England Journal of Medicine*.

The matter of rebuilding of practices and the regaining of patients is a personal, local matter. The subcommittee urges that doctors in a community take pains to inform patients acquired during the war years with the fact that their doctor has returned from the service. The subcommittee believes that no official action of the Society is appropriate in this connection.

It is of importance that all veteran physicians inform themselves on the various activities of the Society in their behalf. Many members of the Society have been in contact with younger graduates

who have not yet become fellows. It is important that these young men be brought into the Society as soon as they have fulfilled the requirements. Who better can bring this before them than those members with whom they served?

* * *

All the preceding was accomplished by the work of the original small committee. At the annual meeting a group of veteran doctors held a meeting to see what further could be done for veterans. At the suggestion of this group each district was asked to appoint a representative to attend a meeting of the Subcommittee on Veterans' Affairs on June 24. At this meeting it was suggested that the original committee be enlarged to include at least one representative from each district. This was promptly accomplished, since the president of the Society was present and immediately appointed the representatives present. There was a long and free discussion of all veteran problems, from which concrete proposals emerged for further action on the part of this subcommittee. These may be briefly summarized as follows:

Education. It was suggested that the course at Sanders Theater be repeated (this has already been planned for) and that courses throughout the state outside of Boston be increased in number and more widely spread. It was also suggested that a two-week graduate course of intensive character be provided at some favorable spot where vacation and work could be combined—something in the nature of a medical Chautauqua. Camp Edwards was suggested as a place for such a course. (This suggestion will be submitted to the subcommittee on graduate education for consideration.)

Automobile procurement. It was decided to write to the larger companies to see if it is possible to secure priority for veteran physicians needing new automobiles.

Hospital seniority. This was discussed at some length. Contact will be made with the Massachusetts Hospital Association to discuss what steps can be taken to assure returning doctors of their former staff priority.

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(Not set on page xxi)

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A Report of Nine Cases

LOUIS WEINSTEIN, M.D., Ph.D.†

BOSTON

INFECTIONS with *Haemophilus influenzae* in children constitute a serious problem. In adults, because of the presence of large amounts of potent bactericidal antibodies in the blood, this organism is much less frequently an instigator of disease processes.¹ During the pandemic of influenza in 1918, however, there were many cases in which the hemophilic organism was isolated from the lungs. It therefore appears that the normally present humoral protection against *H. influenzae* may break down under certain conditions and that this type of infection may be of great importance in all age groups. In children, there is no part of the respiratory system that is immune to invasion by this bacterium, and regardless of the location of the disease, the process is always serious and produces a high mortality rate unless promptly and efficiently treated. The other important type of infection produced by *H. influenzae* is meningitis, occurring most frequently between the ages of three months and two or three years, practically all these cases are due to organisms belonging to Type B of Pittman.²

The mortality rate in untreated cases of *H. influenzae* meningitis is between 92 and 100 per cent for all age groups. Weiss and Huntington³ found the death rate to be 80 per cent in a group of 127 patients who were more than two years of age. Treatment with horse serum alone, with horse serum and complement and with sulfonamides alone or in combination with horse serum has produced little effect, and according to Fothergill,⁴ the mortality rate ranges from 54 to 82 per cent in patients receiving these types of therapy. The most effective method of treatment of influenzal meningitis is

that devised by Alexander.⁵⁻⁷ This consists of the use of rabbit serum containing antibody against Type B organisms together with sulfadiazine. With this therapeutic regimen, the mortality rate was reduced by Alexander to 26 per cent in a group of patients ranging in age from three months to over five years, in those over seven months of age, the death rate was only 18 per cent.⁸

Although the results obtained by the use of type-specific antiserum and sulfadiazine are striking, there are still an appreciable number of deaths from influenzal meningitis treated in this manner. Furthermore, the employment of heterologous serum always carries with it the risk of immediate or late reaction owing to hypersensitization. The development of a nontoxic, nonsensitizing, easily given chemotherapeutic agent that can cure influenzal meningitis in as great a percentage as that achieved by Alexander's method or, if possible, in a larger number of cases of the disease appears to be most desirable.

In 1944, Schatz, Bugie and Waksman⁹ reported the isolation of a new antibiotic agent from *Streptomyces griseus*, streptomycin, which was active against some gram-positive and many gram-negative organisms. Birmingham¹⁰ has shown that *H. influenzae* is inhibited by streptomycin in a range of 1:56 to 5 gamma. Little information is as yet at hand regarding the effectiveness of streptomycin in the therapy of *H. influenzae* infections in man; but several reports have appeared in the literature indicating that this agent may be of value in such cases. Birmingham¹⁰ and Smith¹¹ have both reported recovery from influenzal meningitis following administration of streptomycin alone. The use of insufficient doses of the drug appeared to lead to the development of drug fastness in the causative organism. Both these investigators believe that the optimal treatment of influenzal meningitis should comprise streptomycin combined with sulfadiazine or serum or both and that the antibiotic agent should be given both intramuscularly and

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committee believes that every effort should be made by hospitals to grant staff appointments, even though of temporary nature or on the courtesy staff, to qualified doctors so that the profession will not be in the position of penalizing men for having spent from two to five years in the services. Already the president of the Massachusetts Hospital Association has sent communications to all hospitals of the Commonwealth urging that particular consideration be given to qualified veteran doctors applying for staff appointments. This supplements similar letters sent long before V-J Day by the Postwar Planning Committee to hospital superintendents, chiefs-of-staff and presidents of boards of trustees of all Massachusetts hospitals. It is earnestly hoped that all hospitals will co-operate in this important matter.

The matter of office space and homes, although acute everywhere, has not appeared to be insurmountable. It is a local problem that has almost invariably yielded to industrious search on the part of the returning veteran. Often he has not been able to secure exactly the type of office and home that he desires, but he has been able to get some type of satisfactory arrangement. The subcommittee urges that each physician having ample office space share it with a returning doctor until such time as the veteran is able to find an office for himself.

Because of the shortage of paper, telephone directories cannot be printed so often as in prewar days, consequently, some physicians will have to wait for some months before being listed. In conferences with the subcommittee, representatives of the telephone company have been most sympathetic and co-operative. The problem, however, is large and involves not only doctors but also other professional and business groups. The best solution at the moment is that returning doctors, when established, take steps to inform their patients of their new address and telephone number. The telephone company has increased its information service and states that within twenty-four hours of the installation of a telephone, the number can be secured through such service. Detailed information on this point was published in the April 18, 1946, issue of the *New England Journal of Medicine*.

The matter of rebuilding of practices and the regaining of patients is a personal, local matter. The subcommittee urges that doctors in a community take pains to inform patients acquired during the war years with the fact that their doctor has returned from the service. The subcommittee believes that no official action of the Society is appropriate in this connection.

It is of importance that all veteran physicians inform themselves on the various activities of the Society in their behalf. Many members of the Society have been in contact with younger graduates

who have not yet become fellows. It is important that these young men be brought into the Society as soon as they have fulfilled the requirements. Who better can bring this before them than those members with whom they served?

* * *

All the preceding was accomplished by the work of the original small committee. At the annual meeting a group of veteran doctors held a meeting to see what further could be done for veterans. At the suggestion of this group each district was asked to appoint a representative to attend a meeting of the Subcommittee on Veterans' Affairs on June 24. At this meeting it was suggested that the original committee be enlarged to include at least one representative from each district. This was promptly accomplished, since the president of the Society was present and immediately appointed the representatives present. There was a long and free discussion of all veteran problems, from which concrete proposals emerged for further action on the part of this subcommittee. These may be briefly summarized as follows:

Education. It was suggested that the course at Sanders Theater be repeated (this has already been planned for) and that courses throughout the state outside of Boston be increased in number and more widely spread. It was also suggested that a two-week graduate course of intensive character be provided at some favorable spot where vacation and work could be combined—something in the nature of a medical Chataqua. Camp Edwards was suggested as a place for such a course. (This suggestion will be submitted to the subcommittee on graduate education for consideration.)

Automobile procurement. It was decided to write to the larger companies to see if it is possible to secure priority for veteran physicians needing new automobiles.

Hospital seniority. This was discussed at some length. Contact will be made with the Massachusetts Hospital Association to discuss what steps can be taken to assure returning doctors of their former staff priority.

All agreed that the most important function of the Subcommittee was to discuss problems that confronted the medical veterans. To this end all veterans are urged to communicate any problems or suggestions that they think are worthy of study or susceptible of solution by Society action to the district representative on the committee or directly to the chairman. The list of district representatives who have been appointed appeared in the July 11 issue of the *Journal*.

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The purpose of the work reported here was to determine the effect of streptomycin on the clinical course of influenzal meningitis, to study the rate of disappearance of the causative organism from the blood stream and spinal fluid and to note any toxic effects that might result from the use of large amounts of the drug.

METHODS

Streptomycin therapy was not started in any patient until the diagnosis of meningitis due to *H influenzae* was established by bacteriologic methods. In a few cases, the causative agent was detected on direct examination of the spinal fluid by the production of capsular swelling with Type B antiserum. In several cases, because of the absence of organisms in gram stains of centrifuged sediment of the spinal fluid, it was impossible to make an etiologic diagnosis until two to three days had elapsed. It was not deemed justifiable to withhold all therapy in cases in which the causative organism could not be detected early in the course of the illness, because all the patients had obvious purulent meningitis. Therefore, chemotherapy other than streptomycin was given until *H influenzae* was isolated, but a period of at least twenty-four to forty-eight hours was allowed to elapse without any type of treatment before streptomycin was given. In this way, it was hoped to avoid treating patients with more than one agent at a time. In all the cases in which treatment was withheld for twenty-four to forty-eight hours, the presence of *H influenzae* in the spinal fluid was confirmed before streptomycin was started.

Streptomycin was administered by two routes, intramuscularly and intrathecally, in a daily dosage of 120,000 to 1,000,000 units by the former route and one of 10,000 to 100,000 units by the latter. The intramuscular injections were spaced at three-hour intervals and each consisted of 15,000 to 125,000 units, whereas the intrathecal ones contained 10,000 to 100,000 units and were given once every twelve to twenty-four hours. Treatment was continued for seven to nineteen days intramuscularly and for at least four to seven days longer intrathecally. Samples of serum and spinal fluid were obtained for determination of levels of streptomycin, and these data will be reported later.

Cultures of the spinal fluid, blood, nose and throat in beef-heart-infusion broth and agar containing added yeast extract, tryptose peptone and blood were made daily during the course of strepto-

mycin therapy and at frequent intervals after treatment was stopped. All the cultures were incubated at 37°C under increased carbon dioxide tension for at least seven days before being discarded as showing no growth. All the organisms resembling *H influenzae* morphologically were identified by the production of capsular swelling with Type B antiserum except in the cases due to a nontypable strain.

All patients treated with streptomycin were observed in the hospital for a period of at least two weeks after therapy had been stopped and were seen two to six weeks following discharge to note whether they developed any sequelae.

CASE REPORTS

CASE 1. C. W., a 5-year-old girl, was admitted to the Haynes Memorial Hospital with a chief complaint of vomiting and stiff neck of 24 hours' duration. She had been perfectly well until the evening before admission, when she began to vomit after every attempt to take food or water. A physician who was called prescribed sulfadiazine which was not retained because of the vomiting. During the night, the temperature rose to 105°F, there were slight convulsive movements and the patient complained of severe headache. On the morning of entry to the hospital the neck was stiff, the temperature was 103°F, and the patient was delirious.

Physical examination revealed the temperature to be 103°F, the pulse 140, and the respirations 22. The nose was moderately obstructed, but the mucous membrane was not inflamed. The pharynx was mildly injected, but the tonsils were not enlarged or reddened. The neck was stiff, and there was a moderate degree of cervical lymphadenopathy. The lungs, heart and abdomen were within normal limits. All the deep and superficial reflexes were present, normally active and equal on both sides. Plantar response was flexor. Kernig's sign was markedly positive bilaterally, and there was marked stiffness of the back.

The urine on admission was within normal limits. The hemoglobin was 9.3 gm, and the white-cell count 32,400, with 87 per cent neutrophils, 4 per cent lymphocytes and 9 per cent monocytes. Lumbar puncture or admission revealed an initial pressure equivalent to 160 mm of water, with free dynamics. There were 6000 cells, 98 per cent of which were polymorphonuclear leukocytes. The total protein was 250 mg per 100 cc and the sugar 26 mg. A gram stain showed long and short pleomorphic gram-negative rods, which did not swell with Type A or B anti-influenza serum. Blood culture on admission yielded the same bacterium. Subsequent bacteriologic studies revealed the organism to be *H influenzae*, belonging to neither Type A nor B.

Immediately after admission, the patient was given 3 gm of sulfadiazine per day, with resulting blood levels of 10 to 24 mg per 100 cc. On this treatment, the clinical condition improved gradually, signs of meningeal irritation lessened, and the white-cell count fell, but the temperature remained elevated. The spinal fluid during the first 2 weeks in the hospital showed a return toward normal, but the cultures remained positive for *H influenzae* for the first week and a half. Late in the 2nd week, there developed a maculopapular itching rash that was thought to be due to the sulfadiazine. No therapy was given for 3 days, during which time the temperature was elevated, the patient again appeared extremely ill, and the spinal fluid cultures grew the gram-negative organism. Sulfamerazine, in doses of 1.5 to 2.0 gm per day, was therefore given, and for a week the temperature was more or less within normal limits, but one spinal fluid examination during this time still revealed the presence of the causative bacteria. On about the 10th day of treatment, the patient began to develop a fever and a maculopapular rash, and the drug was stopped for several days, during which the temperature returned to normal. After 4 days without any chemotherapy, however, the temperature suddenly rose to 104°F and sulfamerazine was again given. For the next 3 weeks,

in spite of sulfamerazine blood levels ranging between 12 and 24 mg per 100 cc, there was a daily elevation of temperature to a high degree, and spinal-fluid and blood cultures revealed the gram-negative pleomorphic rod. The patient again appeared quite ill, had marked anorexia, was very listless and showed signs of moderate meningeal irritation. Streptomycin treatment was started at the end of the 8th week in the hospital. A dose of 5000 units was given

The patient was observed in the hospital for 3 weeks after streptomycin was stopped, and several lumbar punctures carried out during this period were all within normal limits.

CASE 2 H. M., a 3-year-old girl, was admitted to the hospital with an illness that began the day prior to admission with nasal discharge, anorexia, irritability and sensations of chilliness. Later, sore throat and pain in the side

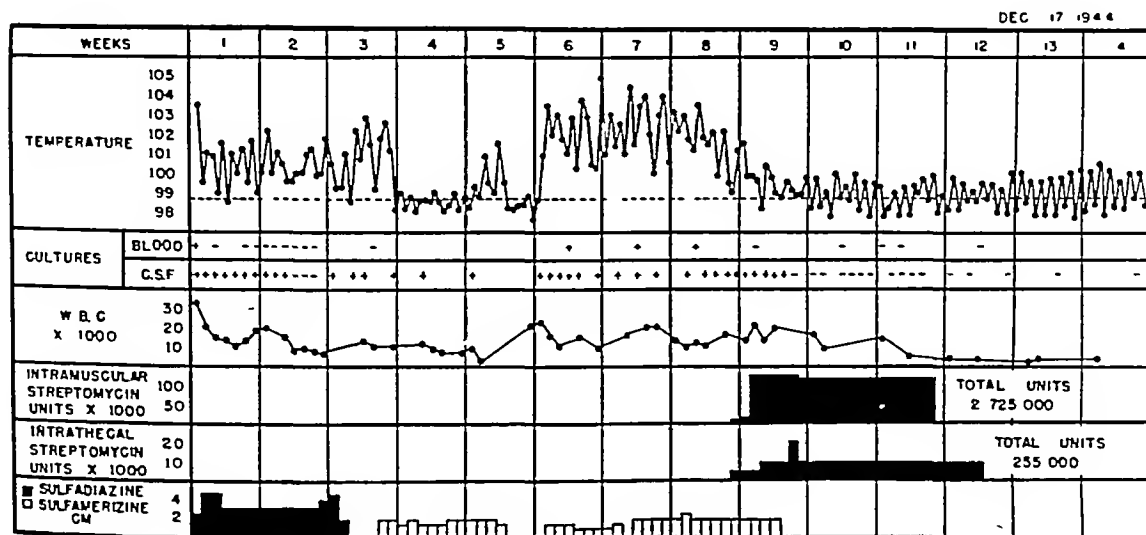


FIGURE 1 Summary of Data in Case 1

intrathecally every twenty-four hours for the first three days and one of 10,000 units by the same route thereafter, the total dose being 255,000 units in 23 days. Shortly

of the neck developed, the respirations became labored, there was difficulty in swallowing water, and vomiting occurred. A dose of penicillin was given, and the patient was referred

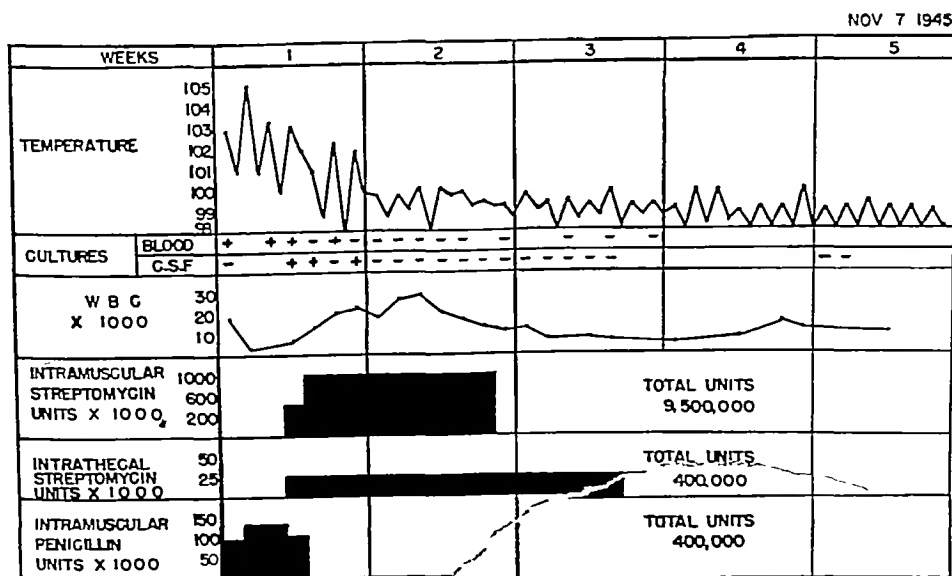


FIGURE 2 Summary of Data in Case 2

after therapy with the antibiotic agent was started, the temperature returned to normal, the white-cell count fell, and the blood and spinal-fluid cultures became negative. There was a concurrent rapid improvement in the clinical condition.

to the hospital with a possible diagnosis of poliomyelitis. Physical examination on admission revealed a well developed, well nourished child who appeared acutely ill and held her head rigidly backward, resisting any attempt at flexion of the neck. The temperature was 102.8°F,

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were lymphocytes. The sugar was within normal limits, and the protein was 39 mg per 100 cc. No organisms were seen on smear. Since the etiology of the meningitis was unknown the patient was treated with 1.5 gm of sulfadiazine a day. Lumbar puncture repeated the next day showed essentially the same findings as on the day before.

On the 4th day, the cultures of the spinal fluid made on the 2nd and 3rd days were found to contain Type B *H. influenzae*. Sulfadiazine administration was stopped, and the patient was given no treatment for 24 hours. Streptomycin therapy, 125,000 units every 3 hours intramuscularly and 25,000 units every 24 hours intrathecally, was started and continued for 9 days by the former and for 3 days longer by the latter route.

There was rapid clinical improvement, and the abnormalities in the spinal fluid soon disappeared. *H. influenzae* was never isolated from the nose, throat or blood.

CASE 4 W. S. L., a 3-year-old boy, was admitted with a chief complaint of convulsions of 24 hours' duration. One week prior to admission he had sustained a contusion on the back of the head as the result of a fall, and subsequently developed fever, nausea, vomiting and abdominal pain. He was treated for the next 5 days for gastroenteritis.

424 lymphocytes per cubic millimeter. The sugar was 59 mg per 100 cc, and the protein 87 mg, but no bacteria were seen on direct examination of a centrifuged specimen. Nose, throat and blood cultures revealed no *H. influenzae*. Cultures of the spinal fluid showed no growth after 24 and 48 hours. Because of the obvious purulent meningitis and the failure to discover the causative organism at the time of admission, the patient was given 3 gm of sulfadiazine a day. On this regimen the temperature remained elevated, the patient continued to appear acutely ill and opisthotonos persisted.

On the 4th day, because growth of the spinal-fluid cultures could not be detected by the ordinary methods, the supernatant was removed from the blood broth and centrifuged at 3000 r.p.m. for 30 minutes. Examination of the sediment revealed that *H. influenzae*, Type B, had been present in the spinal fluid from the time of admission. All therapy was omitted for the next 24 hours, during which time the temperature rose to its highest point 103°F. On the 6th day, when the white-cell count was 31,000 and the temperature 103.8°F, treatment with streptomycin was begun. A dose of 100,000 units was administered intrathecally initially and doses of 25,000 units were given every 24 hours thereafter for 14 days. In addition a dose

DEC. 13, 1945

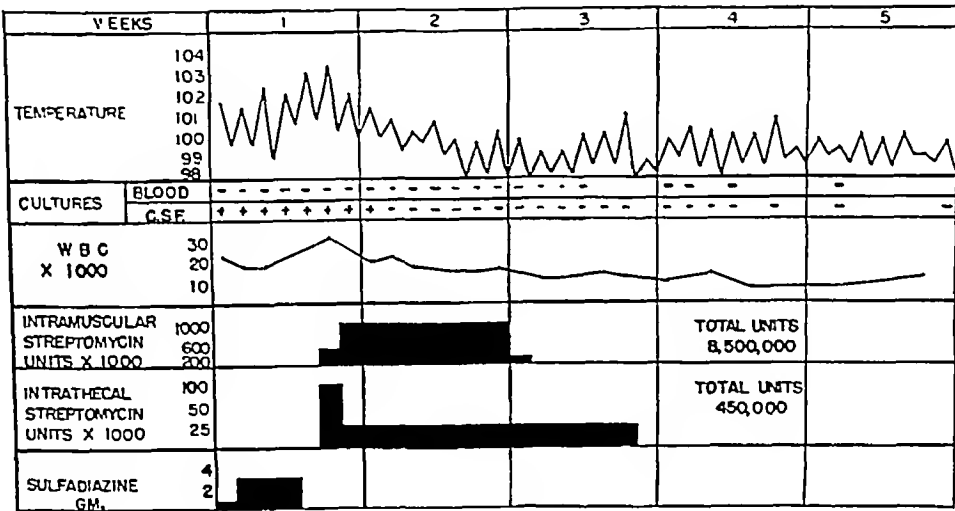


FIGURE 4 Summary of Data in Case 4

but because vomiting and convulsions occurred 5 days after the fall, he was admitted to an outlying hospital for observation. Physical examination at that time revealed the patient to be acutely ill and in poor contact with his surroundings. The only neurologic finding was a moderate degree of opisthotonos. Twenty-four hours later, marked restlessness and delirium appeared and lumbar puncture yielded a reddish-colored spinal fluid under markedly increased pressure. Penicillin intrathecally and intramuscularly and sulfadiazine produced no improvement in 24 hours, and the patient was referred to this hospital.

Physical examination on admission revealed a well-nourished, well-developed boy who was in marked opisthotonos, restless and irritable and appeared extremely ill. The temperature was 100.6°F, the respirations 24, and the pulse 152. The mouth was dry, and the tongue coated. The neck and back were markedly stiff, with the head held in extreme extension, and the patient protested violently against any attempt at flexion. Kernig's sign was markedly positive bilaterally. The abdominal reflex in the left lower quadrant could not be elicited. The remainder of the examination was normal.

The urine on admission was within normal limits. The hemoglobin was 14.1 gm. The white-cell count was 22,900, with 72 per cent neutrophils, 26 per cent lymphocytes and 2 per cent monocytes. Lumbar puncture yielded a spinal fluid that contained 543 polymorphonuclear leukocytes and

of 125,000 units was injected every 3 hours intramuscularly for 10 days.

Shortly after the beginning of streptomycin therapy marked improvement in the clinical course was noted, and the patient was completely recovered 15 days after treatment was begun. Spinal-fluid cultures became negative 2 days after streptomycin was given, and the chemical and cellular abnormalities of the fluid rapidly disappeared. Numerous blood cultures made during the course of the disease were sterile.

CASE 5 S. A., a 15-month-old girl, was admitted with a chief complaint of convulsions of 12 hours' duration. One week prior to admission, the patient developed a "cold" which was quite mild for the first few days but was followed by diarrhea consisting of several loose, nonbloody stools a day until 24 hours before entry. The next morning, the patient was irritable, refused to sit up and developed generalized twitchings. On admission to an outlying hospital, she was found to have a stiff back and neck, a temperature of 102°F, and a positive Kernig's sign bilaterally. The white-cell count was 19,500, and lumbar puncture yielded a spinal fluid that contained 4500 cells per cubic millimeter. Penicillin was immediately given intrathecally and intramuscularly, but when bacteriologic examination of the spinal fluid several hours later revealed Type B *H. influenzae* anti-influenza serum was administered in doses of

the pulse 120, and the respirations 26. On the right side of the neck, behind the right mandibular angle, there was a small, hard, tender swelling that was surrounded by edema. There was enlargement of the tonsillar node on the left. The remainder of the physical examination was within normal limits. Kernig's sign was negative bilaterally, and stiffness of the back was not striking.

The white-cell count was 17,500, with 64 per cent neutrophils, 32 per cent lymphocytes and 4 per cent monocytes. The urine was essentially normal. The spinal fluid was under normal pressure and contained 10 lymphocytes and 6 polymorphonuclear leukocytes per cubic millimeter, the sugar and protein levels were normal and culture yielded no growth.

Shortly after admission the temperature rose to 105°F, and a dose of 15,000 units of penicillin was given intramuscularly every 3 hours. At the end of 18 hours, the temperature had decreased to 100.8°F, but it fluctuated between

consistent with early bronchopneumonia. *H. influenzae* was isolated from nose and throat cultures for the first time on the 21st day. At discharge 34 days after admission, the patient showed no sequelae except moderate generalized weakness.

CASE 3. L. A., a 2-year-old girl, was admitted with an illness that had begun 3 weeks previously, with mild obstruction of the nose and a high degree of fever. Because of the finding of moist rales in one of the lungs, treatment with one of the sulfonamides had been given for 4 days. Thereafter, fever recurred and the sulfonamide was readministered, but failed to produce any beneficial results. The patient was therefore admitted to a hospital for further study 4 days prior to admission to this hospital.

At the outlying hospital a large number of white cells were found in the urine. Treatment with penicillin resulted in some improvement. On the night before admission

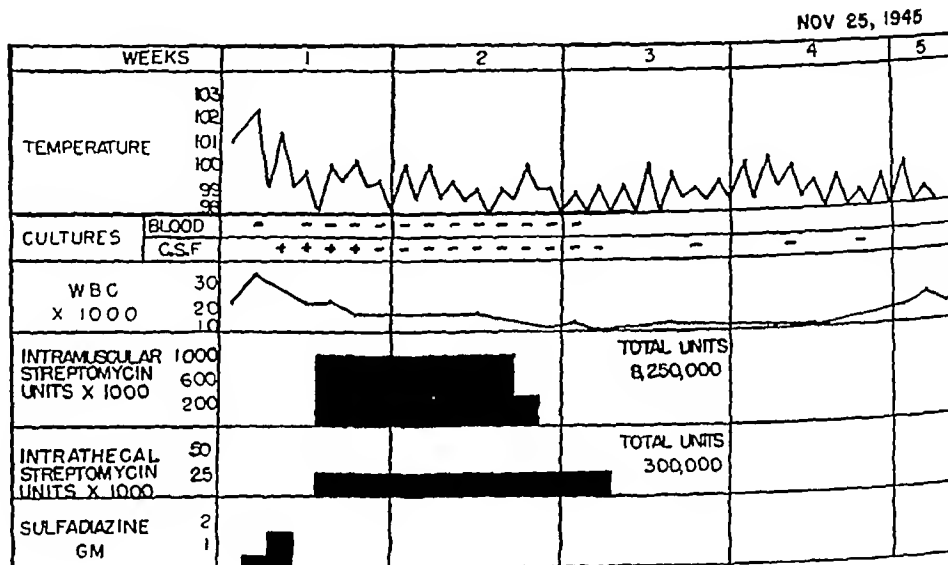


FIGURE 3 Summary of Data in Case 3

101 and 105° for the next 3 days. On the 4th day, marked stiffness of the neck, back and hamstring muscles and positive Kernig signs became evident. The spinal fluid was under increased pressure and contained 1100 white cells per cubic millimeter, with 82 per cent polymorphonuclear leukocytes and 18 per cent lymphocytes. The sugar level was 21 mg per 100 cc and the protein level 63 mg. Type B *H. influenzae* was identified on direct examination.

Penicillin was stopped and a regimen of 25,000 units of streptomycin intrathecally once every 24 hours and 125,000 units of streptomycin intramuscularly every 3 hours was instituted. The temperature fell rapidly and by the 8th day had reached normal limits, where it remained during the rest of the hospital stay. The cell count in the spinal fluid gradually decreased, and the cultures for *H. influenzae*, which were twice positive during the first 3 days of streptomycin treatment, became negative on the 4th day and remained so thereafter. There was marked improvement in the patient's clinical condition, and all signs of meningeal irritation had disappeared at the end of 6 days of streptomycin treatment. The drug was continued both intramuscularly and intrathecally for 10 days, and by the latter route alone for 6 days longer.

The white-cell count, which fell to 4000 on the 2nd day, rose to 28,000 on the 10th day and returned to a normal level on the 16th day, where it remained for the rest of the period of observation. Blood cultures were positive for *H. influenzae* on the 1st, 3rd, 4th, and 6th days only once after the start of streptomycin treatment. X-ray examination of the chest on the 5th day revealed findings

to this hospital, stiffness of the neck and a rise in temperature to 103°F developed. Lumbar puncture yielded a clear fluid under increased pressure. The patient was transferred to another hospital with the diagnoses of pyelonephritis and meningitis, type undetermined, having received 25,000 units of penicillin and 2 gm of sulfadiazine just before discharge. At the second hospital, a rash was noted and the patient was sent to this hospital with a possible diagnosis of scarlet fever.

Physical examination on admission revealed a pale girl who appeared to be chronically ill. The temperature was 100.4°F, the pulse 128, and the respirations 28. The skin showed a moderate degree of hyperkeratosis follicularis over the chest and abdomen. The remainder of the examination was within normal limits except for a few moderately enlarged anterior cervical lymph nodes. There were no signs of meningeal irritation or increased intracranial pressure except for slight tightness of the hamstring muscles bilaterally. The remainder of the neurologic findings were essentially normal.

The white-cell count on admission was 22,150, with 55 per cent neutrophils, 45 per cent lymphocytes and 1 per cent monocytes. The urine was normal except for 5 to 10 white cells per high-power field of a centrifuged specimen. Shortly after admission, the temperature rose to 102.4°F and slight stiffness of the neck and increased spasm of the hamstring muscles became apparent. Lumbar puncture revealed increased pressure of the spinal fluid, which contained 389 cells per cubic millimeter of which 54 per cent were polymorphonuclear cells and 44 per cent

could be cultured. All blood and spinal-fluid cultures made during the time of streptomycin treatment and after the antibiotic substance was stopped were sterile. The patient was kept in the hospital for 4 weeks following the completion of treatment and remained completely well.

CASE 6 H M, a 3-year-old boy, entered the hospital with a chief complaint of fever and vomiting of 12 hours' duration. He had been well until 4 days prior to admission, when he began to suffer with poorly described discomfort in the left ear. No other symptoms appeared until the day before admission, when severe anorexia, fever, restlessness, increased irritability and vomiting were present. A physician who saw the patient on the following day found him to have a temperature of 103°F and a stiff neck and referred him to the hospital.

Physical examination on admission revealed a well developed, well nourished boy who was comatose and responded only to extremely painful stimuli. The temperature was 102°F, the respirations 36, the pulse 124, and

drug was administered intramuscularly every 3 hours in doses of 100,000 units for 10 days and intrathecally every twenty-four hours in doses of 25,000 units for 14 days.

The clinical course was marked by rapid improvement, so that within 1 week the patient appeared to be completely recovered. A rise in temperature to 102°F on the 21st day occurred, with an acute suppurative otitis media, from which a hemolytic *Staphylococcus aureus* but not *H. influenzae* was isolated. This condition subsided without any treatment in a few days. After therapy was started, cultures of the blood were never positive and those of the spinal fluid revealed the causative organism only once. Daily cultures of the nose and throat revealed Type B *H. influenzae* — for the first time on the 29th and 30th days.

CASE 7 W V, a 4-month-old boy, was admitted because of convulsions of 24 hours' duration. The present illness began 10 days prior to admission, when the patient

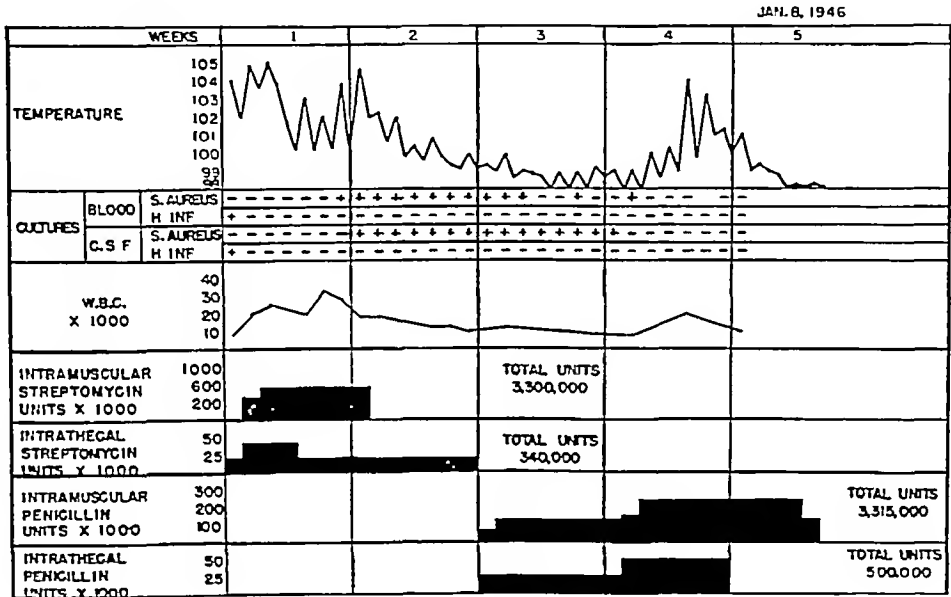


FIGURE 7 Summary of Data in Case 7

the blood pressure 75/40. In the skin over the medial aspect of the lower left leg were several small, edematous, papular areas, the tops of which were crusted. The left ear drum was diffusely reddened, but the landmarks could be made out easily. The eyes moved aimlessly. The pharynx and tonsils were markedly reddened but no exudate was seen. The neck and back were extremely stiff. Neurologic examination was essentially negative except for absent abdominal reflexes and a strongly positive Kernig's sign bilaterally.

The urine on admission was entirely within normal limits. The hemoglobin was 16.2 gm. The white-cell count was 7950, with 79 per cent neutrophils, 16 per cent lymphocytes and 5 per cent monocytes. Lumbar puncture on admission revealed an initial pressure equivalent to 480 mm. of water, with normal dynamics, and the spinal fluid contained 3650 cells, 99 per cent of which were polymorphonuclear leukocytes. The protein was 250 mg. per 100 cc., and the sugar 54 mg. A gram stain showed pleomorphic gram-negative rods that proved to be Type B *H. influenzae* both by direct typing and by culture. Blood cultures yielded the same organism.

Because of an error in the bacteriologic diagnosis on the original examination of the spinal fluid, the patient was given 15 gm. of sulfamerazine intravenously. When the presence of *H. influenzae* was detected 1 hour later, streptomycin, 50,000 units intrathecally and 100,000 units intramuscularly, was given immediately. Thereafter, the

developed a mild upper respiratory infection, which had an uneventful course until the 4th day, when the temperature rose to 103°F. The patient did not appear particularly ill, but on the next day the temperature was 104°F. Examination by a physician at that time revealed nothing of note, and treatment with an antipyretic led to a fall in temperature to 100°F for 24 hours. The next day the temperature was 103°F and the patient was given one of the sulfonamide drugs; this produced a moderate degree of improvement. On the day before admission, the patient began to have generalized convulsive seizures, which rapidly increased in frequency and duration until they were present almost constantly at the time of entry to an outlying hospital, where a lumbar puncture revealed cloudy spinal fluid containing gram-negative pleomorphic bacteria. Because of this finding, the child was referred to this hospital for treatment.

On admission the patient was a well developed, moderately obese infant who held himself rigid, with all the extremities in flexion and the head in extension. The temperature was 102.2°F, the respirations 32, and the pulse 130. The anterior fontanelle was wide open and bulging. The lower part of the right tympanic membrane was red, and the light reflex and visibility of the bony landmarks were diminished. The eyes followed a bright light to the right but not to the left. The nose contained a small amount of purulent exudate, and the mucous membrane was reddened. The pharynx was slightly reddened.

5 cc intravenously and 6 cc intrathecally. The patient was referred to this hospital for further treatment.

Physical examination on admission revealed a well developed, well nourished child who was pale and irritable, breathed rapidly with grunting respirations and stared vacantly into space. The temperature was 104°F, the pulse 180, and the respirations 60. The left eardrum appeared thick and injected. The nose revealed a small amount of mucopurulent exudate. The pharynx was

Because of the rapid fall in temperature and the general clinical improvement, as well as the negative blood and spinal-fluid cultures, all therapy was withheld for the first 3 days. At the end of this time, spinal fluid withdrawn on the 2nd day was found to contain *H. influenzae*, sulfadiazine, 3 gm per day orally, was therefore started. Lumbar punctures on the 8th, 10th, 12th and 13th days made while the patient was receiving sulfadiazine, revealed *H. influenzae*. All therapy was then stopped for 48 hours.

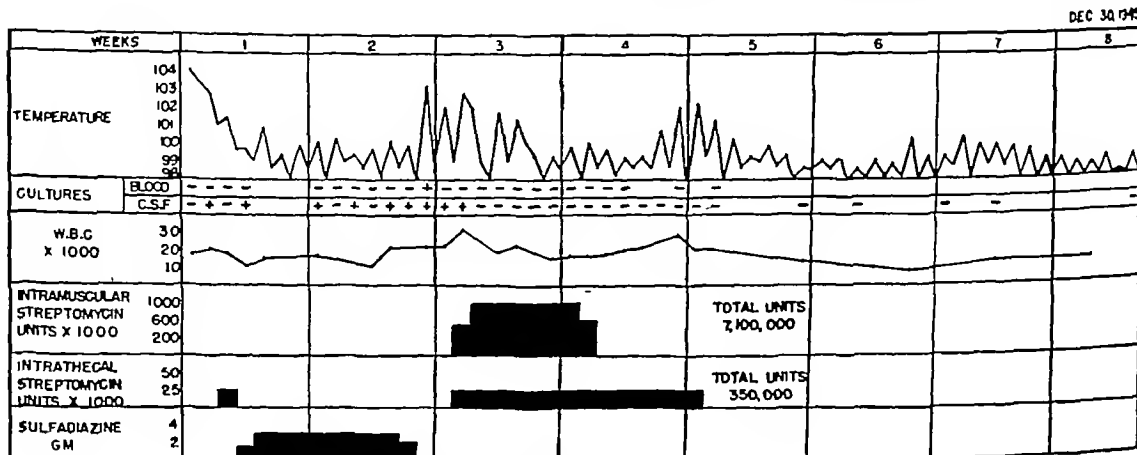


FIGURE 5 Summary of Data in Case 5

moderately injected, the tonsils were slightly enlarged, and a thick, purulent postnasal discharge was present. The neck and back were moderately stiff. The neurologic findings were within normal limits except for a slightly positive Kernig's sign bilaterally. The remainder of the examination revealed no abnormalities.

The white-cell count on admission was 16,850, with 45 per cent neutrophils, 52 per cent lymphocytes and 3 per cent monocytes. The urine was within normal limits

during which time the temperature rapidly rose to fluctuate between 99 and 103°F. The patient again appeared acutely ill, and blood and spinal-fluid cultures grew out the hemophilic bacteria.

Streptomycin, 25,000 units intrathecally every 24 hours and 125,000 units intramuscularly every 3 hours, was first administered on the 16th day and was continued for 8 days by the latter route and for an additional 6 days by the former route. Within a short time after the initiation of

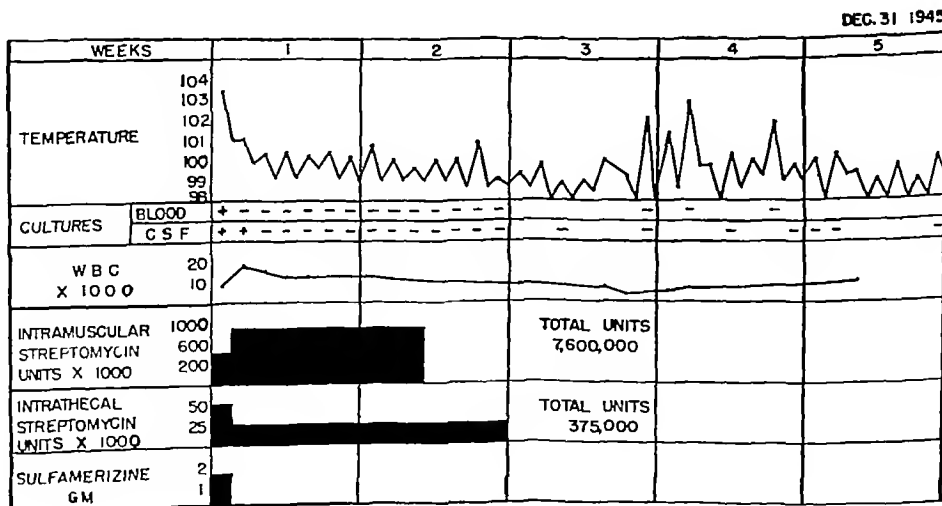


FIGURE 6 Summary of Data in Case 6

except for a specific gravity of 1.032. The hemoglobin was 11.6 gm. Examination of the spinal fluid revealed 165 polymorphonuclear leukocytes, 3000 lymphocytes and 5000 erythrocytes per cubic millimeter, the protein was 252 mg per 100 cc, and the sugar 65 mg. Gram stains and cultures of the spinal fluid on admission were negative for *H. influenzae* or any other organism.

this treatment, the temperature returned to within normal limits and marked improvement in the general clinical condition was noted. The spinal fluid showed a rapid return to normal. A mild elevation of temperature from the 27th through the 30th day was concomitant with a bout of diarrhea consisting of several loose, nonbloody stools a day, from which no pathogenic enteric organisms

to twelve green, watery stools a day, had been present. Four days before entry, the patient had a "cold" and showed difficulty in swallowing. During the next few days, she became drowsy, and just before admission began to have twitchings of the right side of the head and frothed at the mouth.

Physical examination revealed a pale, emaciated girl who held her eyes wide open and her neck in slight extension. The temperature was 101°F, the pulse 150, and the respirations 30. The arms and legs were semirigid and flexed. There was marked looseness of the skin over the whole body. There was a small amount of purulent exudate in the nose. The neck and back were stiff. The lungs were clear except for coarse rhonchi throughout. All reflexes were physiologic. There was a thick, purulent vaginal discharge. The remainder of the physical examination was within normal limits.

The white-cell count on admission was 25,000. The urine was normal except for a large number of white cells. The hemoglobin was 9.3 gm. A lumbar puncture revealed increased pressure, and the fluid contained 910 cells per cubic millimeter, 80 per cent of which were polymorphonuclear leukocytes. The total protein was 95 mg per 100 cc, and the sugar 34 mg. Direct examination revealed gram-negative pleomorphic rods resembling *H. influenzae* but not typable with either Type A or B serum. Culture of the vaginal discharge yielded *Proteus vulgaris* and colon bacilli. The blood was sterile. An untypable strain of *H. influenzae* was isolated from the pharynx.

Immediately after admission, the patient was started on a regimen of 100,000 units of streptomycin intramuscularly every three hours and was given 50,000 units of the same agent intrathecally. Intramuscular therapy was con-

On the 9th day, the rectal temperature dropped to 95°F and the patient died, respirations ceasing 10 minutes before the heart stopped.

Autopsy There was hydrocephalus with marked destruction of brain tissue and many areas of fibrin, particularly about the base, from which a nontypable *H. influenzae* was isolated.

The strain of *H. influenzae* isolated from the patient was subsequently found to be susceptible to 1.25 units of streptomycin per cubic centimeter (cup method, with the Merck strain of *Staph. aureus* as the control). Concentrations of streptomycin considerably larger than this were presumably present in the spinal fluid at all times.

DISCUSSION

Nine cases of acute purulent meningitis due to *H. influenzae* were treated with streptomycin, with good results in 7 cases. In 7 cases the organisms belonged to Type B, whereas in the other 2 the bacteria were neither Type A nor B. Bacteremia was present in 7 cases at the time the meningitis was first diagnosed. The age of the patients infected with the Type B organisms varied from four months to three years, whereas the children from whom the nontypable strains were recovered were four months and five years old, respectively.

Two of the patients died. One, aged ten months, was infected with a Type B organism that disappeared from the spinal fluid and blood after twenty-four hours of streptomycin treatment. This patient subsequently developed a *Staph. aureus* bronchopneumonia and succumbed in spite of intensive penicillin therapy. At autopsy the brain revealed only two small plaques of fibrin on the cerebral hemispheres, cultures were sterile. The other patient succumbed to persistent influenza bacteria infection, which showed no response to treatment with large amounts of streptomycin. *H. influenzae*, type unknown, was cultured from the brain at autopsy.

It was the purpose of the work reported herein to determine the value of streptomycin alone in the treatment of influenzal meningitis. In every case in which prior treatment with sulfonamide or other agents had been given, a period of twenty-four to forty-eight hours without therapy of any type was therefore allowed to elapse before streptomycin was administered, to eliminate the possibility of treating with two agents at the same time and also to assure the presence of active, progressing infection. It is problematical whether prior treatment with sulfadiazine had any favorable influence on the later effectiveness of streptomycin. It is noteworthy that, in every case in which the sulfonamide was used, organisms were constantly present in the spinal fluid in spite of adequate blood concentrations of the drug. In some of the cases, however, there was some degree of clinical improvement during the period of sulfadiazine therapy. This may indicate that the infection of the meninges had been partially inhibited but not eradicated by the administration of sulfonamide, this possibility is borne out by the fact that omission of all therapy

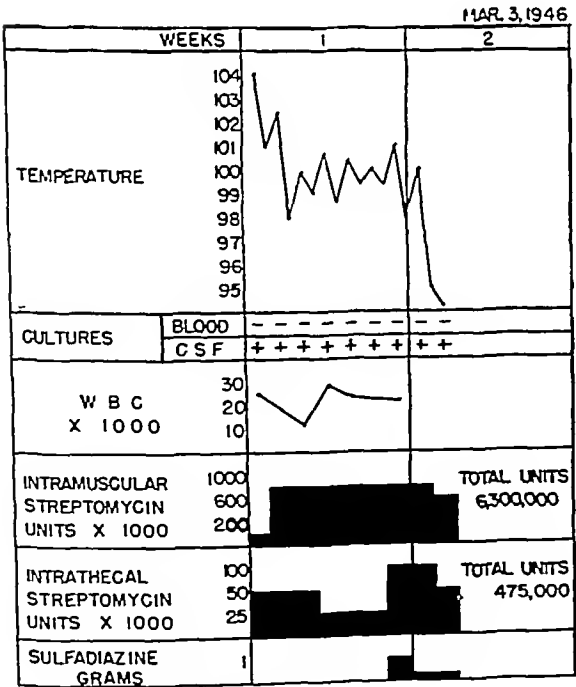


FIGURE 9 Summary of Data in Case 9

tinned for 8 days. After the initial intraspinal dose, a dose of 25,000 units was given every 24 hours for 3 days and one of 50,000 units every 12 hours for the remaining 2½ days.

The patient rapidly lapsed into coma, showed generalized twitchings and convulsions almost constantly and had persistent fever. The white-cell count remained high. Spinal-fluid cultures revealed the presence of *H. influenzae* on each of twelve examinations carried out over a period of 8 days. Cultures of the blood were repeatedly negative.

but otherwise normal. The neck and back were extremely rigid. Kernig's sign was markedly positive bilaterally. The examination was otherwise within normal limits.

The urine on admission was normal except for a slight amount of albumin. The white-cell count was 8500, with 46 per cent neutrophils, 49 per cent lymphocytes, 3 per cent monocytes and 2 per cent basophils. The hemoglobin was 11 gm. The spinal fluid was under increased pressure and contained 36,400 cells per cubic millimeter, 91 per cent of which were polymorphonuclear leukocytes. The sugar was 30 mg per 100 cc, and the protein 50 mg. Many gram-negative pleomorphic rods that exhibited capsular swelling with Type B anti-influenza serum were present. Cultures of the spinal fluid, blood and nose were positive for Type B *H. influenzae*. This organism could not be demonstrated in the pharynx.

Immediately after the etiology of the meningitis had been established, a dose of 20,000 units of streptomycin was administered intrathecally. Twenty-four hours later, drug administration by the intramuscular route in doses of 50,000 units every 3 hours was also started. Therapy was continued by intramuscular injection for eight days and intrathecally for 5 additional days. During the 2nd, 3rd and 4th days, because of failure to improve clinically, intraspinal injections of 20,000 units of streptomycin were given every twelve hours. The spinal fluid and blood cultures became negative for *H. influenzae* within 24 hours after therapy was instituted. The convulsions, twitchings, stiff neck and positive Kernig's sign disappeared after 11 days of treatment.

On the 8th day, the temperature rose to 104.6°F. Blood and spinal fluid cultures, which had been made daily, showed a coagulase-positive hemolytic *Staph. aureus* continually from the 7th day onward, but because the organisms grew very slowly and the first three cultures were considered to be possible contaminants, the diagnosis of staphylococcal meningitis and bacteremia was not made until 1 week after onset. *Staph. aureus* was present in the nose in pure culture on the 8th day. In spite of the new infection of the meninges, the clinical condition was improving rapidly except for the appearance of a scarlatiniform rash over the entire body from the 10th to the 12th day.

Because spinal-fluid and blood cultures were persistently positive for *Staph. aureus*, penicillin was given intrathecally, 25,000 units every 24 hours, and intramuscularly, 15,000 units every 3 hours, for the first 8 days, when the amount administered by each route was doubled because spinal-fluid and blood cultures still revealed the causative organism. Following the increase in dose of the antibiotic agent, these cultures rapidly became negative.

A febrile episode on the 26th day was probably related to an upper-respiratory infection, since redness of the pharynx and a watery nasal discharge were present at this time.

Type B *H. influenzae* was isolated from the throat in pure culture several times after recovery from the influenzal meningitis. The patient was observed in the hospital for 2 weeks following the cessation of penicillin treatment and showed no residua or sequelae of the meningeal infections. This part of the course of the illness is not included in Figure 7.

CASE 8 C G, a 10-month-old girl, became ill 2 days prior to admission, when she cried much more than normally and became quite drowsy. On the day before entry, she began to vomit, appeared pale, was quite warm and slept almost constantly. Later in the day, when stiffness of the neck and a temperature of 103°F were noted, the patient was referred to this hospital.

Physical examination revealed a well developed, well nourished girl who was extremely restless, breathed rapidly and emitted frequent high-pitched cries. The temperature was 105.6°F, the pulse 150, and the respirations 44. She reacted readily to painful stimuli. The anterior fontanelle was normal. There was an internal strabismus of both eyes. The neck and back were stiff. Kernig's sign was negative. There was a small area of consolidation in the midportion of the right lung posteriorly. The remainder of the physical examination was within normal limits.

The white-cell count on admission was 10,850, with 70 per cent neutrophils, 29 per cent lymphocytes and 1 per cent monocytes. The hemoglobin was 12.3 gm. The spinal

fluid was under increased pressure and contained 18,250 cells per cubic millimeter, 80 per cent of which were polymorphonuclear leukocytes. The protein was 114 mg per 100 cc, and the sugar 26 mg. Direct examination revealed gram-negative pleomorphic rods that gave capsular swelling with Type B anti-influenza serum. The blood culture revealed Type B *H. influenzae*. Nose and throat cultures were negative for *H. influenzae*.

Treatment with streptomycin was started immediately after admission. A dose of 100,000 units was given intr

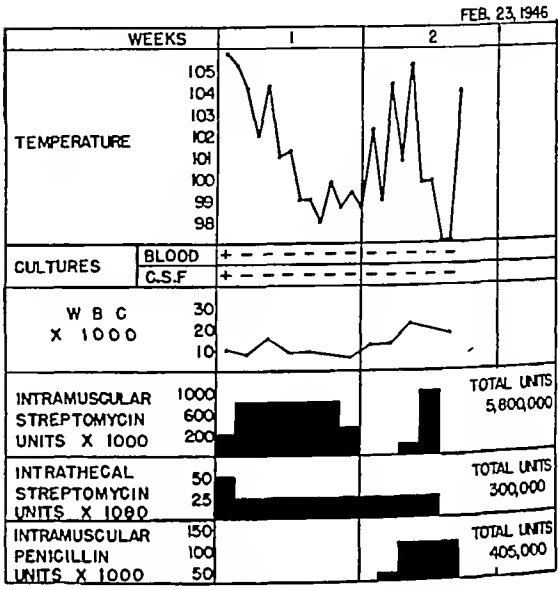


FIGURE 8 Summary of Data in Case 8

muscularly every 3 hours for 5½ days. After a period of 2 days with no treatment, the drug was again given and 1,200,000 units was administered in the next 30 hours. Fifty thousand units of the antibiotic agent was instilled into the spinal canal on admission, and 25,000 units was given every 24 hours thereafter for the next 10 days.

The blood and spinal-fluid cultures revealed no organisms 24 hours after the beginning of treatment, and none were recovered during the remainder of the course. The clinical condition improved somewhat in that the temperature reached a normal level on the 5th day, but coma and twitchings persisted. On the 5th day, a pure culture of *Staph. aureus* appeared in the nose and throat, and this organism was isolated every day thereafter. On the 8th day, the temperature suddenly rose to 102°F, and it remained at high levels for the rest of the course. Physical examination at that time revealed no abnormalities, but on the following day moist, crackling rales were heard throughout both lung fields and x-ray examination revealed diffuse bilateral bronchopneumonia. Since it was thought that this was probably due to *Staph. aureus*, the patient was treated with penicillin, 15,000 units being given intramuscularly every 3 hours for the next 4 days. The patient remained in coma, convulsions became more frequent and severe, the temperature continued to be elevated, and death occurred on the 12th day. Blood cultures grew out *Staph. aureus* during the last two days of life.

Autopsy The brain was within normal limits except for two small plaques of fibrin, one on each of the cerebral hemispheres, bacteriologic studies were negative. The lungs showed a diffuse confluent bronchopneumonia from which a coagulase-positive hemolytic *Staph. aureus* was isolated.

CASE 9 K B, a 4-month-old-girl, was admitted with a history of having had a bronchopneumonia, which responded to one of the sulfonamides, 2 weeks previously. For 1 week before admission, diarrhea, consisting of seven

SUMMARY AND CONCLUSIONS

Nine cases of purulent meningitis due to Type B *Haemophilus influenzae* in 7 and to an untypable strain in 2, were treated with streptomycin, with complete recovery in 7 cases. The drug was given intramuscularly in doses ranging from 15,000 to 125,000 units every three hours and intrathecally in amounts varying from 10,000 to 25,000 units every twenty-four hours.

Two of the 9 patients with influenzal meningitis treated with streptomycin died. One showed complete absence of response to the antibiotic agent. The other died of an intercurrent *Staphylococcus aureus* bronchopneumonia, which was not affected by penicillin.

The blood and spinal fluid were cleared of the causative organisms in twenty-four to forty-eight hours in all cases except the 2 due to atypical strains.

No relapses or sequelae of the influenzal meningitis were observed in any of the recovered patients over a period of six to ten weeks following the cessation of streptomycin treatment.

No toxic reactions attributable to streptomycin were observed in the nervous, hematopoietic or urinary systems.

Two of the patients receiving streptomycin developed infections, in one case meningitis and in the other bronchopneumonia, — both with bacteremia, — due to *Staph aureus* after they were completely free of *H influenzae* in both the spinal fluid and blood for several days and were apparently recovering clinically.

Since *Staph aureus* infections may occur as complications during treatment with streptomycin, careful watch must be maintained for early signs of this type of involvement. The use of penicillin as soon as *Staph aureus* becomes the predominant organism in the nasopharynx, even before the evidence of invasion is present, is strongly recom-

mended. The possibility of administering penicillin and streptomycin together from the time treatment is started suggests itself.

Streptomycin appears to be the drug of choice in the treatment of meningitis due to *H influenzae*. It should be administered by both intrathecal and intramuscular routes. There seems to be no need to combine the antibiotic agent with one of the sulfonamides or with type-specific antiserum unless no beneficial effects result from the use of large amounts of streptomycin given for at least seventy-two to ninety-six hours.

Addendum Another patient with meningitis due to Type B *H influenzae* has recently been treated with streptomycin. This four-year-old boy recovered after treatment for six days by the intramuscular and ten days by the intrathecal route, the causative organism disappearing from the cerebrospinal fluid in less than twenty-four hours. Recovery was complete and no sequelae were evident six weeks after discharge from the hospital.

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rapidly produced increased severity of clinical manifestations, bacteremia and an increase in the abnormal changes in the spinal fluid

The portal of entry for *H influenzae* infection in most cases appeared to be the upper respiratory tract. In 2 cases, otitis media was present, in neither of these, however, were the gram-negative bacteria isolated from the ear. In 6 cases *H influenzae* was isolated from the pharynx and nose. It is interesting that in 2 of these cases the organisms could not be recovered until after the patients had been treated with streptomycin and were recovering from the meningitis.

The dosage and time of administration of streptomycin were chosen more or less arbitrarily. In Case 1, relatively small amounts of the drug were injected because only little of the material was available. In the other 8 patients between 800,000 and 1,000,000 units was given daily in divided intramuscular doses every three hours. Every patient received, in addition, between 20,000 and 100,000 units of the drug intrathecally because, as has been shown by Anderson and Jewell,¹³ streptomycin does not enter the spinal fluid in appreciable amounts when injected either intramuscularly or intravenously. The usual procedure was to give 50,000 or 100,000 units intrathecally when treatment was first started and to instill 25,000 units every twenty-four hours thereafter. In two cases, it was considered necessary to give the drug more frequently by the intrathecal route, in these cases it was administered every twelve hours for several days. The total dosage of streptomycin for the entire period of treatment varied between 2,725,000 and 9,500,000 units intramuscularly and 225,000 and 475,000 units intrathecally. Whether the quantity of streptomycin used in the cases reported was larger than that actually necessary to cure influenzal meningitis can be determined only from experience with the use of smaller doses. The possibility of administering the antibiotic agent by the intrathecal route alone in cases of meningitis due to *H influenzae* suggests itself, but such a procedure appears too risky, because about 70 per cent of patients with this disease have concurrent bacteremia. Reduction of the length of time over which intramuscular therapy is given seems more feasible because, in most cases, the blood was found to be sterile after twenty-four to forty-eight hours of treatment.

In most cases, the rapidity with which both spinal fluid and blood were rid of *H influenzae* following the administration of streptomycin is extremely striking. Of the 8 patients treated with large doses, the spinal fluid was free of the hemophilic bacteria in 2 cases in less than twenty-four hours and in 5 between twenty-four and forty-eight hours. In 1 case, the organisms never disappeared. In the patient given relatively small doses of the

drug, ninety-six hours was required before sterilization of the spinal fluid was accomplished. Disappearance of the infecting organisms from the blood stream was even more rapid than that from the spinal fluid. In only 1 case was bacteremia still present twenty-four hours after the beginning of treatment, in all the others the blood was free of bacteria in less than twenty-four hours. The fact that large amounts of streptomycin do not prevent the establishment of a new infection by an organism not susceptible to the drug is illustrated by the 2 patients who developed *Staph aureus* meningitis and bronchopneumonia with bacteremia while undergoing treatment for the *H influenzae* infection. No toxic effects directly related to streptomycin were observed.

The development of severe infections with *Staph aureus* in 2 cases is worthy of note. It is striking that in both these cases the organisms appeared in pure culture in the nasopharynx before they invaded more deeply. It is possible that streptomycin, by altering the relation of the various organisms in the pharynx, may, in some situations, allow relatively insusceptible organisms like *Staph aureus* to increase rapidly in numbers and virulence. The use of penicillin in combination with streptomycin for the treatment of gram-negative infections suggests itself as a possible procedure in avoiding late complications by infection with gram-positive organisms. The necessity for careful frequent study of the nasopharyngeal bacterial flora in patients being treated with streptomycin seems apparent, and the use of penicillin when many gram-positive pathogenic organisms such as *Staph aureus* make their appearance, in an attempt to prevent invasion by these bacteria, seems strongly indicated.

All the recovered cases treated with streptomycin were observed on the wards for two to four weeks following cessation of therapy, and in no case were sequelae of the infection or the treatment observed. Several of the patients were in good health two to six weeks after leaving the hospital.

Although the number of patients treated is small, the present study indicates that, in most cases, streptomycin is an effective agent in the treatment of meningitis and bacteremia due to *H influenzae*. The results obtained compare favorably with those following the use of type-specific antiserum and sulfadiazine. The employment of streptomycin in cases of *H influenzae* infections obviates any danger inherent in serum therapy and eliminates the necessity for frequent titrations to demonstrate excess antibody levels. It also precludes the occurrence of toxic reactions that may result from sulfadiazine. So far as can be determined, streptomycin is without appreciable toxic effect in man. When available in sufficient quantities, it seems to be the drug of choice in the treatment of disease produced by *H influenzae*.

We want to put in a good word for the corporals. They are willing to co-operate and are helpful. They are a swell bunch of guys. We are leaving this morning and we thought we should let them know we appreciate all the kindness we received from them — and we also enjoyed your talks.

Is this publicity on the awful conditions in veterans' hospitals true, and if not why do they print such stuff?

Dear Doctor I am a single man and I am deeply in love with a lovely lady back home. Doctor, I am getting up in age. I have had intercourse with this girl several times, and have never been able to satisfy her although we have tried again and again, but yet she still wants to marry me. Do you think it would be possible for us to have a happy married life?

Doctor Would you try to clear this question for me. During the night I wake up a few times and each time when I awaken it takes me a good ten to thirty seconds to remember where I am at. When I am trying to remember where I am at it's like a nightmare.

Dear Doctor At the present time I'm reading *A Tree Grows in Brooklyn* and I was quite surprised when the author states that several of the women characters loathed the thought of sleeping with their husbands. I have been married several years and this came as quite a shock to me. Is this common in married life? Why do women stay with their husbands if they feel this way? The only thing I find wrong with your talks is the fact that they are not nearly long enough. I would like to sign this but don't want to be accused of "ear hanging" so I'll just sign — "a patient, a fan and I feel as though I can say, a friend."

I have a problem which concerns myself as well as many others. This problem is of intermarriage. I am privately engaged to a Protestant girl and I am Jewish. I do love her very much, and vice versa. We are really in love, doctor, and the only thing preventing me from taking her hand in marriage is the matter of our children. Her father is dead, but her mother is living and my folks are living. I do love her and after being away twenty-eight months I want to marry her. Please give us some help and suggest a way to bring up the children which would be easy for all concerned. We both believe in God and because we were born to different faiths shouldn't prevent us from marriage. What religion should we teach the children? Thank you in advance. Please give us assistance.

Dear Doctor Is it possible for a homosexual person to control his emotions and lead an ordinary sex life or is he in that state mostly because he prefers to be? Is it true that intercourse after pregnancy can cause a person to be "homo" or are our reactions, likes and dislikes the reasons for homosexuality? Can a doctor help a person who sincerely wants to be helped, and what is the remedy?

Doctor, I have had a tachycardiac condition for the past year. My diagnosis is psychoneurosis anxiety. I would like to know how these two things are related and what I can do consciously to cure this ailment. During this year overexertion, excitement and stimulants have been the causes for recurrences of this heart condition. Should I leave these things alone or will each, in a proper amount, help me to effect a cure?

Dear Doctor My wife has confessed to me that she has gone out with another man during my absence. She says that it was nothing serious, but for a couple of months her letters were cool and distant, although she did write practically every day. She says now she is sorry it ever happened and that she has learned her lesson. She now claims to love me more than ever. Would you speak to her of her "going out" upon returning home, or just forget about it and try to make the best of it? I love her very much.

Doctor I have been in a melancholy state of mind for a year. What part does it play on the brain?

What makes you dream of killing people in your sleep? Is it because you hate someone very much? It always concerns me, and it wakes me up. It scares me an awful lot.

Dreams cause me to awaken with a tired and inner tumbling feeling. What can one do to suppress them? What is the nature and interpretation of a dream? Certain foods seem to be a cause, is that a foundation of fact, or a misconception?

Do worry and nervousness cause ulcers? Does continual irritation of ulcers develop into cancer? Is watch-

ing your diet the only way of healing ulcers? Does stomach trouble cause backaches?

Will you please tell us more about a hysteria neurosis — how it differs from other types of neurosis, why it is harder to overcome and whether it is acquired or hereditary?

At the morning talks I think we should talk about our future problems and what we will do when we are out of the Service instead of talking about women all the time. A lot of us are married and we don't believe our wives are running around, but drops of water on a stone will soon wear a hole.

Doctor Best of luck and an early "gettin' home" to you and your staff. You have all shown a kindness and courtesy which is a credit to the Medical Corps and yourselves. The human treatment and the chance to express themselves openly or in the "gripe box" is as democratic as any procedure I have seen in the Navy. More power to you and your practice.

Dear Doctor As you know, we had a talk on having food in the diet kitchen. The gripe before was about chiefs [chief petty officers] and corporals' eating steaks in the diet kitchen. Our gripe is who in the hell stole our two hot dogs from the refrigerator after we went through a lot of trouble swiping these dogs from the mess hall? As we are heavy eaters we have to have our snack before hitting the sack. Please inform the thief to keep his hands off our chow.

Dear Doctor Tonite is my last nite here at the hospital or I should say school. Because it's been like a school to me. You've helped me a great deal since I've been a [pupil] here, not a patient. You've learned me a great deal about life that I never before knew. By your talks every morning and your smiles that you gave us all every morning at sick call and wherever you meet us. And believe me, Doctor, that smile did me more good than all the medicine anyone could give. I knew at times it was hard to smile, but nevertheless you did. I only hope that the fellows that may enter your school gain as much out of your talks as I have. God bless you always! Keep them smiling, Doctor!

RESULTS

The following objective indications that the patients as a whole have derived considerable benefit from the program form the reason for presenting this article, as well as for continuing the talks.

Daily attendance has averaged 74 per cent. Even after the patients have been transferred to other wards because of crowding, many of them continue to return for the talks. Requests from patients on neighboring wards for permission to attend are frequently received.

At the close of the first week, the patients themselves requested a change of title for the "gripe box" on the ground that after the second day it ceased to contain any gripes. They have now adorned it with the following legends:

Worried? Curious? Troubled? Family trouble? "Dear John" letters? Leave a note for the doctor. Do you have a complaint or question you would like discussed? If so drop a note without your signature. Your medical officer will be glad to discuss any of these with the group each morning.

An unprecedented avalanche of requests for social service and legal assistance with personal problems descended on the local Red Cross department. These questions included illness and hardship at home, delayed news, financial problems and so forth. There was a sharp decrease in the number and frequency of requests to ward nurses and corporals for information — requests that often so dis-

NEW EXPERIENCES IN GROUP PSYCHOTHERAPY*

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THIS paper presents a report on the mass handling of large groups of borderline neuropsychiatric casualties on an open ward in the large naval hospital at Aiea Heights, Territory of Hawaii. The rapid turnover and the mixed diagnoses placed limitations on the program, but the group psychotherapy seems to have been much more important than medication in the rehabilitation of these men.

PROCEDURE

During the month of August, 1945, 285 patients, — seamen, specialists, petty officers and chief petty officers, — with diagnoses including the fatigue states, the various neuroses, some hysterias, somnambulism, mild epilepsy and various personality disorders, spent an average of ten to fourteen days en route from front-line hospitals to the United States. Almost all of them knew that they were headed for a prolonged stay in the United States, if not for an actual medical discharge. The effect of the cessation of hostilities during the middle of the month did not improve their status, nor did it diminish their complaints. On the contrary, there was observed a generalized increase of tension and restlessness, even on non-neuropsychiatric wards, and indeed even among the staff members, including corpsmen, nurses and medical officers. The average daily census on the ward was 115, and the average daily attendance at conferences was 85.

After sick call every morning, during which every patient was seen and given an opportunity to express a complaint, exchange a friendly greeting or make an appointment for a private conference later in the morning, — frequently by request, if he appeared to be unusually worried or ill, — the patients were invited to gather at one end of the ward for an informal talk. An average daily attendance of 74 per cent of these patients attested to the fact that the invitation was welcomed by most of them. They participated vigorously in discussions that covered a wide variety of topics, and often lasted not only well past the allotted hour but sometimes for several successive days. The subjects included health, diagnoses, — medical and surgical as well as neuropsychiatric, — the causes and treatment of the neuroses, insomnia, disturbing dreams, courtship, marriage, insurance, educational opportunities and problems and the Red Cross services.

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Nontechnical language, frequent interruptions for questions or comments, a blackboard and drawings, made by the patients themselves, and the presentation of actual case problems by the patients, usually anonymously, were the rule of the day. Occasionally a patient availed himself of the opportunity to leave the meeting whenever he chose to do so. A so-called "gripe box" was placed in the lobby, and its contents furnished the key to the particular day's discussions. Sample questions and comments are given below.

The average educational level of these men was the tenth grade. About two thirds of the group were married. Attendance on other duties, such as care of gear, special details, consultations and chapel attendance, cut down the average number of sessions attended to six, although many patients managed to be present at a dozen or more.

Some of the questions asked and comments made were as follows:

Could you explain the procedure that is followed when we return to the States? Do people think we are crazy, or what?

Does the pulse beat fewer times than the heart beats? If not, why doesn't it?

Please explain discrimination — not only of race but of color and creed — in the Service and in civilian life and between officers and enlisted men. Aren't some of us being a bit hasty in "judging other people's actions by our own"? To avoid any jumping at conclusions, the writer is white, of German-Dutch-English descent, a Mormon, and has spent quite a few years in both civilian life and in the Navy. Thank you for the help you have given all of us.

Suggest co-operative consideration among men in the Service. I believe this is a basic cause of a great deal of discontentment.

We have heard rumors that they send letters to our people stating that we are in the hospital, and we would like to know what they say if that is true.

What causes ulcers of the stomach, and can they be cured?

If a person in the family died with a cancer, is it possible for anyone else in the family to inherit one, and can they be cured?

How should one go about telling adopted children their status?

If you and your wife are nervous, will your child be nervous too — and what will be the cause?

Will you please explain the diagnosis of psychoneurosis, anxiety, and if we are given a medical discharge will "PN" be stamped on our discharge?

Will duty in the Pacific have any effect on making a person sterile?

What's the cause of talking, walking and screaming in one's sleep? What is the cure for this condition?

Good morning, Doctor. If a man has something on his mind concerning his wife and himself after they are married — something which she *should* know about — will you be so kind as to explain to the group a correct way to inform her about the trouble — the trouble being the couple can't have children — the male at fault, and in this certain case it is the female at fault.

These morning sessions are the bright spot of an otherwise drab routine.

half years as a prisoner of the Japanese. A few of his observations are given as a requisite to understanding the reaction of the neuropsychiatric patients to his story.

Out of about 3500 sick patients — all prisoners of war and most of them Americans — he recalled less than 50 who were neuropsychiatric casualties. The bulk of these were psychotic, and all were given the so-called "cage treatment," which was literal incarceration in an open cage, usually without clothing, with an inadequate supply of food, with no medication whatsoever and with frequently repeated abuse, violence, torment and torture — chiefly beatings, wettings and freezing. Even the vermin-infested mats were denied them for bedding, and they were often deprived of the half-rations usually accorded to other sick patients. When they died, the other patients were forced to stand by and watch their cremation, as a warning not to die — (sick prisoners cannot build airfields, and half-rations are no inducement to remain on the sick list). A temperature of 103°F or higher was required for admission to the sick list. A Japanese "doctor" performed alleged appendectomies without anesthetics (Red Cross supplies were unobtainable because they were needed to fill the black-market demand), and experimented with beriberi and other diseases by injecting intravenously aqueous solutions of whole soy bean preparations. The death of 8 of these unfortunate victims in succession did not deter his "research." The worst psychotic patient the soldier recalled was a homicidal maniac who was convinced that men were bent on killing him. He stood the cage treatment for six weeks, after which he returned to his duties, remaining cured from then on.

"Could you tell us," I asked the speaker, "whether you had many psychoneuroses, and approximately how many and what type?" He shook his head with a sad smile, and said, "They were too sick." Spontaneously his audience of 120 patients burst into honest and uncontrolled laughter.

Evidence of the protracted effects of the group talks can be seen from the following abbreviated reconstructive analyses.

CASE 1 A seaman, first class, with a ninth-grade education, who had been away from home for 2 months, for the first time, was admitted to the sick bay for nostalgia and an anxiety neurosis. After attending seven ward talks, he asked for help in regard to a lump in his throat that had suddenly appeared 3 nights previously.

The patient could think of nothing unusual that had occurred during the day of onset, but readily admitted that a lump in one's throat frequently denoted grief. He laughed at the suggestion that he might be thinking that someone was trying to choke him, and was equally certain that he had no organic disease in his throat.

On the day of onset, the patient had seen the moving picture "Wells Fargo." The scenes that he remembered were those in which the hero's mother-in-law salvaged the note written by her daughter and sent it to the Confederate enemy, causing the ambush and near death of her son-in-law. The patient had been keeping company with a young girl for

several years. He was sure that her mother would object to an early marriage, and was reluctant to admit that the reason he had not mentioned the existence of this girl to his mother was that he feared that she too would oppose the union. He realized that, unlike the hero in "Wells Fargo," a pioneer of the transcontinental delivery service, he was not returning as a hero, but that like him he was returning to a home of ever increasing value. He readily accepted the analogy that just as a problem in arithmetic might have several different answers, all of them correct, so there must be many factors contributing to his neurosis. Before the close of the half-hour interview he was able to apply this reasoning to two other functional complaints — pains in the region of the left breast and speeding up of the heart. His associations were as simple as they were obvious — "heart panic" or "heart ache." He did not know that heart failure was such a frequent cause of death, so that this phase of the interview was not pursued. He dwelt a little more on "heart throb," and left in a smiling and greatly relieved mood. Two weeks later his complaints had not returned, and his clinical status had greatly improved, notwithstanding the delay in his evacuation.

CASE 2 A 22-year-old, unmarried aviation mechanic, who was gaunt and underweight and appeared to be harassed, with a diagnosis of hysteria kept insisting that the pains in his perineum must be organic, and that even though the vertebral x-ray films and prostatic smears were negative, the only treatment that had given him any relief was the prostate massages he had received a few weeks previously. He had had 14 years of schooling.

During the initial examination he was asked whether the term "a pain in the ass" meant anything in particular to him. His response was a spontaneous grin, and he agreed to think over possible associations pending his next interview.

Several days later, and after repeated denials, the patient recalled his first experience of perineal distress. This and succeeding associations during four sessions of 20 minutes each, were as follows. At the age of 15 he visited a hospital where a favorite brother-in-law was recovering from serious mutilating injuries. On entering the hospital he experienced sharp distress in the perineum. The present complaint was similar but more accentuated. He had the same sensation whenever he visited a hospital if he saw anyone who was badly injured. He continued "About ten days ago at a picnic I was O.K. until it came time to come back [to the hospital]. Then it suddenly came back in the buns — I remember seeing a sign, 'Don't throw cigarette butts on the deck.' Yeah, I do sometimes call it my 'buntt.'" During his earlier period of hospitalization he had had to receive rectal tubes for relief of abdominal distention, the relief was pleasant, and eased his perineal distress. The use of the tube recalled his fear of hemorrhoids — from his straining at stool — and his buddies, who had had to have hemorrhoidectomies for painful and bleeding piles about a year previously, at the time of the onset of the present illness. His mother has used an enema daily, and she had not slept with his father for as long as he could remember. Once when drunk he thought that he had accomplished anal intercourse with his mistress, and had been ashamed of this ever since.

On the occasion of the last interview, at which these associations were uncovered, the patient entered smiling and demanded to be returned to duty on the ground that he had recovered. He was advised to take a few months at a convalescent hospital first. He stated that he began to "catch on" after the seventh group lecture — especially after the talk on constipation. On that day he stopped straining in order to test himself for the presence of the pain and suddenly discovered that it had left him. Except for two transient returns following sports, he has remained symptom-free for 3 weeks, for the first time in 11 months.

CASE 3 A 27-year-old, married carpenter's mate with an eighth-grade education had had 11 months of active duty, 7 of them overseas. The diagnosis was anxiety psychoneurosis. After his fifth session on the ward, he asked about a disturbing dream that had occurred on three successive nights a month earlier, causing him to awaken in a tense and anxious state. In the dream a strange man was entering his home in the United States and either kidnapping or killing his baby and assaulting his wife.

rupted the working day that they interfered with routine chores. There was also a noticeable decrease in requests for private interviews with the doctor, as well as a change in the nature of these interviews. Just as the bulk of the questions in the complaint box became predominantly psychosomatic and socio-marital in content, so the bulk of the private consultations became sharply confined to specific problems instead of covering the generalized psychosomatic complaints that formerly predominated. This increased insight is illustrated by the following remarks: "I think I know what caused my headaches, now, but why do they keep coming back on me?" — "That talk you gave on the changes in the stomach and guts when you're scared — well, I guess that's me alright, but what am I scared of now?" — "You mean to say I keep blaming myself for sumpin' I didn't have the nerve to finish way back then?" "But Doc, I tell you I *do* love my father, I — well, yes, there *was* one time when I was pretty mad at him for something he did." A review of some of the questions in the preceding section also gives a fairly accurate picture of the depth of interest and understanding that has been cultivated in these men.

Although there is obviously no way of measuring the effectiveness of abbreviated individual psychotherapy, it seems to have increased. This is shown objectively in the conduct of the men on the wards, their ability to sleep without sedation and their heightened interest in recreational and occupational therapeutic pursuits. This is in sharp contrast to my experience with similar cases on open neuropsychiatric wards where there has been no such group psychotherapy.

Invitations to outsiders to serve as group leaders or as guest speakers have also increased as a direct result of the interest shown by the patients. These guests have included chaplains, Red Cross workers, specialists in education and returning ex-prisoners of war. Some of the specific contributions are presented below.

There has been observed by corpsmen, nurses and the doctors a sharp decrease in the number and frequency of requests by patients for the most frequently used medications — sedatives, cathartics and aspirin. For technical reasons this cannot be proved statistically, but that it is true is attested by the fact that the observation was made spontaneously.

One of the difficulties in obtaining a statistically accurate report of this decrease was the fact that peace came during the first month of this program. One would expect it to have operated as a favorable therapeutic influence, but the fact is that for the first two weeks after the cessation of hostilities there was observed a general feeling of being let down, accompanied by mounting tension and anxiety over the delay of demobilization. This was noticed among the non-neuropsychiatric patients as well,

at times amounting even to actual friction and quarrels between patients and corpsmen. It was also easily discernible among the staff — the psychiatrists not excepted. Despite this, the demands for medication on this ward decreased*.

On one afternoon the irritability and restlessness of patients on two similar open neuropsychiatric wards reached unusual and in some cases almost hysterical proportions. The occasion was the announcement of an evacuation list on which some of the newly arrived patients had been placed, to the neglect of many of the earlier ones. The almost complete absence of such unrest on this ward was the result of a two-minute preliminary talk by the senior corpsman, a pharmacist's mate, second class. He explained that inequities and discrepancies often crept in, and that when a rush order came in for a quota to fill an unexpectedly available ship, some men whose records and disposition had been held up by requests for consultations or for laboratory studies, or on account of accumulations in the record office, might be delayed for a few days longer than others, but that in the long run the selections tended to balance up with reasonable fairness. So long as the patients knew that someone was taking an interest in them, that there was no intentional discrimination or neglect and that someone felt that they were important enough to deserve an explanation, they were reasonably satisfied. This conclusion is justified by the complete absence of complaints about the evacuation list in the complaint box on the following day. A few weeks later, with a new group of patients, when the preliminary talk had been unintentionally omitted, the box was again filled with protests over apparent inequities on the list.

The unsolicited reports of comments and discussions overheard among the patients that keep coming in from corpsmen, nurses and workers in other departments lend confirmation to the impression that the work is constructive. One observer said: "There was a complete absence of sensationalism, smirking or smut in their discussion of the question of whether the couple that had engaged in premarital intercourse should marry, and much of their discussion of intermarriage questions was on a distinctly highly intellectual plane."

PRISONERS OF WAR

In anticipation of the arrival of repatriated prisoners of war from Japan, it was the expectation of the psychiatrists at this hospital that not many psychotic or psychoneurotic patients would be encountered. This anticipation was fully realized.

One of the new arrivals, a pharmacist's mate, second class, was invited to meet with the group on the ward. In an informal way he presented a brief picture of some of his experiences during three and a

*On the closed neuropsychiatric wards there was observed during this same period a pronounced increase of depressed patients and of patients with deep anxieties over guilt as well as of suicidal attempts.

problems. Lecturers, teachers and clergymen of all denominations are learning that their most popular meetings are those in which they give to their respective fields a liberal and human interpretation. Many of these leaders have been conducting group psychotherapy for centuries. Much more of this sort of "treatment" is needed.

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MEDICAL PROGRESS

OPHTHALMOLOGY

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IN the past year there have been no outstanding advances in ophthalmology. Two subjects, however, have been selected on the basis of general interest.

PENICILLIN IN OCULAR INFECTIONS

Enough time has elapsed since the introduction of penicillin to evaluate its efficiency in treating diseases of the eye. The literature abounds with case reports of alleged cures, but in many of these the penicillin has been used along with sulfonamides and other drugs, so that its true therapeutic role is difficult to determine. One fact, however, stands out clearly: penicillin is usually superior to the sulfonamides for several reasons. It is generally nontoxic, whatever route of administration is chosen¹, its antibacterial action is not inhibited by autolytic products and secretions², it has little if any deleterious effects on the regeneration of corneal epithelium³, and it is not incompatible with other frequently used drugs, such as atropine, cocaine, procaine and sulfadiazine.^{4,5} With these advantages it should be the drug of choice in treating any ocular infection known to be due to penicillin-sensitive organisms. Unless, however, certain basic facts are understood regarding its distribution in the ocular tissues by various methods of administration, many cases will not be treated effectively, and much valuable time will be lost before the ocular infection can be brought under control.

In 1944, Struble and Bellores,⁶ using rabbits and dogs, showed that when penicillin was injected intravenously in large amounts it was concentrated in the ocular tissues as follows, in descending order: the extraocular muscles, the conjunctiva, the sclera, the choriorretinal tissue and aqueous. Only a trace was found in the cornea and vitreous, and none was found in the lens. When, however, penicillin was applied locally by corneal bath, a much higher concentration was found in the conjunctiva, sclera,

iris and aqueous than when it was given either intravenously or subconjunctivally.⁷

The same year, von Sallmann and Meyer⁸ showed that repeated instillations of penicillin solution or ointment in the eyes of rabbits produced no detectable antibacterial activity on the part of the aqueous, even with the addition of wetting agents, which usually enhance the passage of various substances through the cornea. A corneal bath, however, resulted in high levels in the aqueous. These investigators also found that by iontophoresis the penicillin passed easily into the aqueous, the latter exhibiting an antibacterial activity for four hours after a single application. The amount recoverable in the aqueous by this method was calculated as being ten times greater than that by the corneal-bath technic.

Leopold and LaMotte⁹ also showed that local instillations were ineffective in getting penicillin into the aqueous of normal rabbits' eyes, on the other hand, this simple method worked quite well when the corneas were abraded or if experimental corneal ulcers had been produced beforehand. The concentrations in the aqueous in these inflamed eyes were well above the required therapeutic level, as defined by Rammelkamp and Keefer,¹⁰ who state that the concentration in serum required for maximum bacteriostatic effect is 0.019 units per cubic centimeter for *Streptococcus haemolyticus* and 0.15 units for staphylococcus. These authors therefore concluded that the elaborate iontophoretic technic was probably unnecessary in dealing with infected corneas when simple instillations appeared to be adequate.

Apparently, intramuscular injections also fail to produce any appreciable concentration of penicillin in the aqueous of normal rabbits, but they may do so when corneal ulcers have been produced beforehand.^{2,8,10}

The application under the lid of a small cotton pack saturated with a solution of penicillin containing 20,000 units per cubic centimeter has been

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For over 10 minutes the patient insisted that he could think of no association, but he finally reluctantly stated that his brother had been unfaithful to his wife and had been caught and forgiven. The patient greatly admired his sister-in-law and felt her wrongs deeply. On the next interview he reported an affair of his own with a former sweetheart and his fear lest his wife should discover it and leave him. One week later he came in to report considerable anxiety over a photograph of himself that he had impulsively sent to the girl friend with an affectionate caption. The picture was sent in June. He regretted sending it at once and requested its return a few days later. An answer was expected in July, but none had yet arrived. The patient reported at the sick bay with his anxiety psychoneurosis on July 15.

It was suggested that even if the unlikely did happen and his wife heard about the episode or saw the picture, there were after all many other things that he had done in June that he did not remember. Apparently the idea of pleading amnesia, together with error, appealed to him, although he rejected it strongly, for 3 days later he reported "I've been sleeping sound the last few days with all the racket—the boys tell me we had a rumpus during the night but I never even heard it." From his account it seemed probable that the picture had been destroyed or would be returned when his mail caught up with him. Insight into the causes of his dream and his bipolar affection for his sister-in-law, together with his exaggerated fear of losing his wife, seems to have been the chief cause of his improvement, which persisted clinically for the rest of his stay of 3½ weeks.

There have been dozens of cases with similar problems, affecting chiefly sleep and functioning of the gastrointestinal tract, that have shown striking improvement, if not recovery, over extremely brief periods of time. Since this improvement occurs in men with a history of continued complaints for months and sometimes years, it is believed that, contrary to popular opinion, it is not necessary to undergo prolonged psychoanalysis or to have a superior education to profit from concentrated psychotherapy.

DISCUSSION

In view of the natural limitations of analytical, hypnotic and narcotherapeutic procedures, and because of the large turnover of borderline neuropsychiatric casualties in this hospital, an attempt has been made to apply the well known principles of group therapy on a somewhat larger scale than has usually been reported.^{1,2}

As was pointed out in a previous paper, there is ample Biblical precedent for the principles of mental hygiene in group therapy.³ The following excerpts from the "Book of Proverbs" bear repetition.

A wise man is strong—by wise counsel thou shalt make thy war, and in multitude of counselors there is safety (24 5-6)

Debate thy cause with thy neighbor himself (25 9)

A scorner seeketh wisdom, and findeth it not (14 6)

He that answereth a matter before he heareth it, it is folly and shame unto him (18 13)

A merry heart doeth good like a medicine [and] maketh a cheerful countenance (17 22, 15 13)

A man that hath friends must show himself friendly, and there is a friend that sticketh closer than a brother (18 24)

Chasten thy son while there is hope, and let not thy soul spare for his crying (19 18)

Labor not to be rich (23 4)

A good name is rather to be chosen than silver or gold (23 1)

Withhold not correction from the child, for if thou beatest him with a rod, he shall not die (23 13)

A man's gift maketh room for him, and bringeth him before great men (18 16)

A brother offended is harder to be won than a strong city, and their contentions are like the bars of a castle (18 19)

It is better to dwell in the wilderness than with a contentious and an angry woman (21 19)

These and similar proverbs, one of which was posted each day on the bulletin board, gave both strength and dignity to our discussions of the commonly accepted teachings of mental hygiene. The majority of the men appear to have learned in an average of half a dozen sessions that a diagnosis of psychoneurosis is not a permanent stigma, that it is a valuable safety valve, and that as such it is a promising and constructive key to a better understanding of their personalities. They readily grasped the idea that any organ may act as a safety valve, and that when the valve was released through a functional disorder—that is, when a neurosis appeared,—three facts were immediately known both to the patient and to the doctor: first, that the inside (emotional) pressure was too great, second, that the valve was functioning normally, and third, that the boiler—the body and brain—was being saved from immediate damage.

A gratifyingly large number of men have reported, without solicitation, that they have noticed a pronounced improvement in health even without follow-up interviews, and often even before they learned of their disposition (evacuation to the United States). Ten patients during the month of August made a sincere request to be returned to duty on the ground that they had fully recovered.

It may be re-emphasized that a great deal of the success of the program is in large measure dependent on the initial interview, in which each patient is given a brief but adequate neurologic and psychiatric examination and an appraisal is made independently of the data contained in his health record.⁴

CONCLUSIONS

The dignity of human companionship and free discussion as a daily accompaniment of the rehabilitation program is a proved and valuable adjunct to physical, medical, occupational and recreational therapy. The nature of the questions and discussions is excellent proof of the earnest desire of most psychoneurotic patients to understand their problems and to do something constructive about them. Limitations of intelligence and education do not seem to be a barrier to the execution of such a program. Much depends on the group leader, but almost any person, whatever his profession, may start such a program if he understands the dynamics of human behavior and maintains a sympathetic attitude toward psychosomatic problems. For such subjects as he may not feel qualified to discuss there will always be experts who will be willing to contribute what they can. For patients of any class it is important that they shall feel that their emotional and personal problems are just as much in need of study and guidance as are their physical and organic

Rycroft²¹ also reported some experimental work with subconjunctival injections of penicillin in human eyes. Ten eyes hopelessly blind and scheduled for removal were given subconjunctival injections of 0.25 cc of a solution of penicillin containing 4000 units per cubic centimeter. After intervals of fifteen, thirty and sixty minutes, aspiration of 0.12 cc of either aqueous or vitreous was performed. It was found that penicillin reached the aqueous after fifteen minutes in 7 of 8 cases. Three of 6 cases showed penicillin in the vitreous after forty-five minutes.

Quantitative determinations on human eyes were made by von Sallmann.¹¹ He selected four eyes about to be enucleated for various conditions—two for malignant melanomas near the disk, one for absolute glaucoma and one for an old injury from an intraocular foreign body. In three eyes he inserted under the lid cotton packs soaked with a solution of penicillin containing 20,000 units per cubic centimeter for one hour. Aqueous determinations showed 2.3 units of penicillin in one case of melanoma and zero units in the other. In the case of absolute glaucoma 9 units per cubic centimeter was found. In the remaining eye, that with the old injury, 4 drops of a solution of penicillin containing 20,000 units per cubic centimeter were instilled and the eye was enucleated two hours later. The aqueous contained 0.5 units per cubic centimeter. Hence, observations on human eyes have been erratic, but generally speaking the average amount of penicillin found in the aqueous is much less than that found in rabbits' eyes.

The weight of experimental evidence indicates the following recommendations for treating eyes infected with penicillin-sensitive organisms. First, intramuscular and intravenous injections of penicillin probably have little effect in controlling infections of the anterior and vitreous chambers. Second, subconjunctival injections may have some effect on infections of the anterior chamber but are probably worthless in infections of the vitreous. Third, infections of the vitreous can probably be most effectively treated by a single intravitreal injection of 0.1 cc of penicillin solution containing not more than 500 units. Fourth, infections of the anterior chamber are likely to be controlled by local application of saturated cotton packs or by iontophoresis. Corneal bath and subconjunctival injection will probably be less effective. In cases of perforating corneal injury with damage to the lens, a single injection of 0.1 cc of a solution of penicillin containing not more than 500 units may be justified. Lastly, for conjunctivitis and infected corneal ulcers, frequent instillations of penicillin drops or ointment will probably be effective. Saturated cotton packs under the lids, iontophoresis or corneal bath should be tried in extremely severe cases.

So much for the experimental work. Case reports of the clinical use of penicillin fill the literature. The

most striking ones deal with cures of gonorrheal conjunctivitis.²²⁻²⁵ Apparently this disease may be effectively treated either by frequent local instillations or by intramuscular injections alone, since the original work of Struble and Bellows⁶ showed that systemic treatment resulted in high concentrations in the conjunctiva. When the cornea is involved, however, it seems wise to use local applications in addition to intramuscular or intravenous injections.

Although no definite dosage or frequency of application has been determined for surface infections, the tendency has been toward higher concentrations and more frequent applications. Thus, Sorsby and Hoffa²⁶ report 47 cases of ophthalmia neonatorum, most of them due to the gonococcus, in which the best results were obtained by using penicillin drops (2500 units per cubic centimeter) every thirty minutes for the first three hours, every hour for the next twenty-four hours, and every two hours for the next two days. Under this regime 21 of 22 cases received a complete clinical cure within one hundred hours. In other groups of cases treated with lower concentrations and less frequent applications, no such high percentage of cures was obtained.

Marginal blepharitis appears to be a condition in which penicillin can be of great value. The usual procedure is to rub penicillin ointment containing 1000 units per gram into the lid margins three times daily. Florey, McFarlan and Mann²⁷ report 48 cases treated in this manner. Cure was complete in three to ten weeks, no other treatment being used. A follow-up of these patients after a year without treatment showed that 66 per cent remained free from recurrences.

Orbital cellulitis has been successfully treated by Sloane²⁸ with the use of intramuscular injections.

The reports of the treatment of corneal ulcers are encouraging. Juler and Young²⁹ and Cashell³⁰ report series in which a rapid cure was obtained in the great majority of cases by frequent instillation of penicillin drops containing 500 units per cubic centimeter.

There have been several favorable reports³¹⁻³⁵ on the direct injection of penicillin into the anterior chamber for infections following perforating injuries. In some cases dramatic improvement has taken place after all other methods aimed at the control of the infection have failed. A single injection of 100 units has usually been sufficient.

No reports on intravitreal injections in the human eye have appeared in the literature, but on the basis of experimental work it seems justifiable to employ them in certain cases of vitreous abscess after perforating injuries. One should be careful to limit the injection to 0.1 cc containing 250 units and to place the injected fluid as near as possible to the center of the vitreous, so that little if any contact is made with the retina.

shown by von Sallmann¹¹ to be extremely effective in producing high concentrations in the aqueous, cornea and iris

The intravitreal penetration of penicillin has been the subject of much experimental work. According to Leopold,¹³ intramuscular and intravenous injections of as much as 4000 units per kilogram of body weight have failed to produce detectable concentrations in the vitreous of normal rabbits. The results following subconjunctival injections have not been uniform, one investigator¹² finding fair levels of penicillin in the vitreous of normal rabbits' eyes and others⁶ finding extremely inadequate levels.

The results of these various investigations on normal eyes can now be correlated with some of the experiments designed to test the efficacy of penicillin in combating experimental infection.

Robson and Scott¹³ successfully treated experimentally produced staphylococcal ulcers on the corneas of rabbits by frequent instillations of a penicillin solution consisting of 500 units per cubic centimeter.

Using rabbits, von Sallmann,¹⁴ by introducing 0.05 cc of a diluted broth culture of pneumococcus (Type 3, 7 or 10) into the anterior chamber, produced a standard infection with simultaneous injury to the lens. Treatment by penicillin iontophoresis was begun six and twelve hours later and was continued for two or three days. The infection was checked in all cases, even after twelve hours, whereas the eyes of the control animals went on to destruction.

Von Sallmann¹⁵ repeated the same experiments using various strains of penicillin-sensitive staphylococci. Penicillin applied by iontophoresis six hours after inoculation controlled the infection in 62 per cent of the eyes so treated. An intralenticular injection of *Clostridium welchii* caused a destructive endophthalmitis, which was not influenced by penicillin therapy.

Direct injection of 0.1 cc of penicillin solution—2500 units per cubic centimeter—into the anterior chamber of the normal rabbit's eye has been shown by Dunnington and von Sallmann¹⁶ to be relatively harmless, but more than this may cause serious damage. This method has been made use of by Scobee,¹⁷ who produced perforating corneal injury in a number of rabbits and then infected the anterior chambers with hemolytic *Staphylococcus aureus*. A solution of penicillin containing 500 units per cubic centimeter was then introduced into the anterior chambers on successive days, but this succeeded in controlling only the mild infections, the severer ones not being affected.

Town, Frisbee and Wisda¹⁸ were able to cure experimental streptococcal infection of the anterior chamber of rabbits' eyes by massive doses of penicillin given intramuscularly, provided no injury to the lens had taken place. They point out that in infections of the anterior chamber a direct injection

of penicillin following a withdrawal of aqueous may be dangerous owing to extension of the infection at the site of the needle puncture.

Von Sallmann and his associates^{19, 20} have shown that the normal rabbit's eye tolerates a direct intravitreal injection of 500 units of penicillin. More than one injection or the giving of more than 500 units in a single one may cause serious damage. Since others¹⁰⁻¹² have shown that intravenous injections, subconjunctival injections, iontophoresis and application of saturated cotton packs all fail to produce more than traces of penicillin in the vitreous, von Sallmann²⁰ tried intravitreal injections in experimentally produced vitreous infections of rabbits' eyes. Each of ten eyes received 0.05 cc of a diluted broth culture of a Type 3 pneumococcus introduced directly into the center of the vitreous. Treatment was begun eight hours later by an intravitreal injection of 0.1 cc of penicillin containing 100 units. All ten eyes recovered completely. The same intravitreal injection was found equally efficacious in staphylococcal infections of the vitreous, in which even 10 units of penicillin checked the infection in all ten eyes. The therapeutic effect was, however, greatly enhanced when a dose of 400 units was injected. Leopold¹² also found that experimental staphylococcal infections of the vitreous of rabbits could be halted by an intravitreal injection of 500 units of penicillin.

Subconjunctival injections of penicillin have been found totally ineffective against experimental pneumococcal infection of the vitreous in rabbits by von Sallmann²⁰ and only partially effective against staphylococcal infection by Leopold.¹² Likewise, intravenously administered penicillin has failed to halt experimental vitreous infection in rabbits.

It must be borne in mind that conclusions reached from experiments on animals' eyes do not necessarily apply to human eyes. It is therefore necessary to examine carefully some of the few human experiments available. One of the first of these was made by Rycroft,⁴ a medical officer in the British Eighth Army in Africa. Shortly after death he removed five normal eyes from 5 soldiers who had been receiving large amounts of penicillin intramuscularly. Penicillin assays were carried out on the aqueous and vitreous, but no inhibition of bacterial growth could be detected. These determinations, however, were made six hours after death and fourteen hours after the last administration of penicillin, so that one might not expect any results. Rycroft then removed seven badly damaged eyes from soldiers receiving large doses of penicillin intramuscularly. In these cases the last dose of penicillin had been given within three hours, but even here no detectable amounts could be found in the aqueous or vitreous. It thus appears that although intramuscular injection may be effective in the case of damaged rabbits' eyes, it is not necessarily so in damaged human eyes.

sive changes. Normally it disappears toward the end of fetal life, but occasionally it persists and forms firm connective tissue in back of the lens.⁶⁴ In the 50 cases reported, 30 infants were premature and 20 were full term. Of the premature infants, 28 showed bilateral involvement and 2 unilateral involvement. Of the full-term infants, the involvement was bilateral in 7 and unilateral in 13. Thus, 35 of the 50 cases were bilateral and 15 were unilateral.

Reese and Payne believe that the same factor that precipitates early birth may also cause the eye lesions. Although no convincing evidence is presented, the authors think that maternal infection may be a factor. A history of uterine bleeding was obtained in 12 of the mothers in their series. Maternal infection is known to cause congenital anomalies in the offspring, as has been shown in the connection between rubella during pregnancy and congenital cataracts.⁶⁵

So far as treatment is concerned, many suggestions have been made. If one accepts the theory of the deleterious effect of light, these premature infants should be kept in a dark room for some weeks as a prophylactic measure. Mydriatics may be used not only to put the iris at rest but also to break up posterior synechiae, which often occur.⁶⁶ Miotics may have to be used in the cases in which glaucoma develops.

Attempts to seal off the hyaloid artery with diathermy have been unsuccessful.⁶⁰ Operations designed to establish new vascular connection between the episcleral vessels outside the eye with the ciliary body are of doubtful value.⁶³ Surgical attempts to remove the lens substance and make a vertical cut in the retrolental tissue have resulted in varying degrees of success.⁶⁴ Irradiation has been suggested as a likely means of closing the blood vessels in the fibroblastic tissue.⁶⁶ In a few cases partial retrogression of the opaque connective tissue behind the lens has been observed without any treatment, but the eyes have never developed normally.

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The results of penicillin therapy in nonspecific uveitis have been disappointing, although occasionally favorable results have been reported. The most complete report on this subject is that of Irvine and his associates,³⁶ who treated 56 cases of all types of uveitis with intramuscular injections of penicillin and 8 additional cases by penicillin iontophoresis. Only in 9 cases of iridocyclitis was any significant improvement noted, and this was said to be no greater than would have been expected from the usual forms of therapy.

Syphilitic uveitis may be expected to respond to penicillin, and such has been found to be the case in the report of Klauder and Dublin³⁷ of 3 cases treated with large doses intramuscularly.

According to Darius,³⁸ trachoma has responded favorably to penicillin instillations, but the improvement observed was said to be in no way better or more rapid than that seen with sulfonamides.

The treatment of dacryocystitis has not been satisfactory. Bellows³ states that the discharge becomes sterile but no clinical recovery takes place.

In cases in which doubt exists concerning the nature of the infecting organism, there is no reason why the sulfonamides may not be employed along with penicillin. Although it has been shown that no incompatibility exists between the two drugs, either *in vitro*⁴ or *in vivo*,³⁹ experimental work indicates that the effect of one does not enhance that of the other.³⁹

Sensitivity of the ocular tissues to penicillin has been occasionally reported.^{5, 40-43} This usually occurs in the form of redness and swelling of the lids, although some cases of generalized urticaria have been seen.

RETROLENTAL FIBROPLASIA

Persistence of the embryonic blood supply of the lens, the tunica vasculosa lentis, is occasionally seen in full-term infants.⁴⁴⁻⁴⁸ It is usually unilateral and has been regarded as a purely local disturbance. What appears to be another phase of this disease is a progressive growth of opaque embryonic tissue behind the lens, which occurs, usually bilaterally, in a number of premature infants after birth. The nature and prevalence of this condition are just beginning to be understood, largely through the work of Terry,⁴⁹⁻⁵⁵ who has given it the name of "retrolental fibroplasia."

The syndrome consists of widespread ocular changes related to persistence of the hyaloid artery and tunica vasculosa lentis, to growth of embryonic connective tissue behind the lens and to persistence of the fetal fibrillar vitreous. The typical changes are shallow anterior chambers, microphthalmia, a fetal-blue color of the iris, searching nystagmus and often retinal separation. Glaucoma and cataract may also occur, and spontaneous hemorrhage into the anterior chamber of vitreous has been reported.⁵⁶ The condition has sometimes been mistaken for retinoblastoma.⁵⁷⁻⁶¹

The incidence of this condition is apparently increasing, probably owing to the greater survival rate of premature infants during the last decade. Clifford⁶² of the Boston Lying-in Hospital found that 12 per cent of infants weighing 3 pounds or less at birth developed this disease. Terry,⁵⁵ using this figure along with statistics compiled by the Children's Bureau of the United States Department of Labor on the annual survival rate of 3600 extremely premature infants, has estimated that a minimum of 432 will be blinded by this cause yearly.

How this condition is brought about is the subject of much speculation. Normally the tunica vasculosa lentis consists of a network of blood vessels surrounding the lens.⁶³ The parent vessel of this system is the hyaloid artery. Venous drainage takes place through the pupillary portion of the tunica, the so-called "pupillary membrane," to the anterior surface of the iris. This whole system is designed to nourish the lens at a stage when the aqueous humor has not yet formed. After the ciliary body begins to produce aqueous, the lens has a new source of nutrition and the need for this elaborate vascular system ceases. Normally at eight and a half months the hyaloid system ceases to carry blood.⁶³

Although there is no direct proof of any one of the many possible causes for persistence and overgrowth of the embryonic vascular system, the most tenable theory, according to Terry,⁵⁵ is the effect of precocious exposure to light in these premature infants. This activates the musculature of the iris before the disappearance of the hyaloid vascular system. The resulting disturbance of the blood supply of this region may prevent aqueous from being formed. This in turn leaves the crystalline lens dependent on the hyaloid artery and tunica vasculosa lentis, and thus this embryonic vascular system persists, instead of regressing.

Terry has stressed the fact that retrolental fibroplasia is more than a persistence of the tunica vasculosa lentis, which consists only of blood vessels and contains no connective tissue. The condition under discussion has as its prominent feature an actual overgrowth of embryonic connective tissue, which, Terry believes, takes place to furnish support for an abnormally developed vascular system. Some of his reported cases have not shown this abnormal hyperplasia until some weeks or months after birth.

Unsuccessful attempts have been made to reproduce the disease in animals whose eyes at birth are extremely underdeveloped, such as the rat and the opossum.

A slightly different viewpoint regarding the development of this condition is held by Reese and Payne,⁵⁶ who have recently reported 50 cases. They believe that the retrolental fibroplasia occurs before birth and is chiefly due to persistence of the primary vitreous, which is vascularized mesoderm. This mesoderm may undergo either progressive or regres-

views of the Massachusetts Medical Society regarding how to afford our own veterans the best of medical care outside of veterans' hospitals

We believe that when such a contract is under consideration there should be at hand one or more duly appointed representatives of the Massachusetts Medical Society empowered to approve any minor changes in the fee schedule that might prove advantageous

As part of his committee's report Dr McCarthy submitted a schedule of fees for medical services rendered under the Veterans Administration Medical Care Program. This schedule, as amended by the Council, is given in Appendix No 2. In moving the acceptance of the report, he said that each member of the Council had received it well in advance of the meeting. The motion to accept the report was seconded by Dr Peirce H Leavitt, Plymouth, and it was so ordered by vote of the Council.

Dr Albert A Hornor, Suffolk, moved that the Council go into executive session. This motion was seconded by Dr Elmer S Bagnall, Essex North, and it was so ordered by vote of the Council.

At this point in the meeting the Council went into executive session.

At 5 30 p m Dr Daniel B Reardon, Norfolk South, moved that the Council rise out of executive session. This motion was seconded by Dr Leavitt, and it was so ordered by vote of the Council.

The President announced that the Council had risen out of executive session.

It was moved by Dr Leavitt and seconded by Dr Charles C Lund, Suffolk, that the Council adopt the part of the committee's report dealing with the fee schedule as amended by the Council, with the understanding that any contract that concerns this fee schedule would be reviewed by the Massachusetts Medical Society within a year.

In the debate attending this motion, it was explained by Dr McCarthy that the duration of any contract that the Blue Shield as administrator entered into with the Veterans Administration would be for one year and that, at the end of six months, either of the signatories might make suggestions regarding its revision.

The motion was adopted by vote of the Council.

It was moved by Dr McCarthy and seconded by Dr Reardon, that the Council approve of the plans whereby the hospital expenses of veterans who are being cared for in civilian hospitals be met by the Blue Cross, acting as administrative agent of the Veterans Administration, and whereby the costs of professional services of civilian physicians, who are caring for veterans under the fee schedule adopted be met by the Blue Shield, acting as administrative agent of the Veterans Administration.

In the debate attending this subject, the Kansas Plan was discussed. Under this plan a schedule of fees has been set up and agreed on by the Kansas Medical Society and the Veterans Administration. The medical society furnishes the Veterans Adminis-

tration with a list of physicians willing to serve under the schedule. The Veterans Administration acts as its own administrative agency. The medical society confers with the Veterans Administration from time to time as problems that concern both arise. It was emphasized that no actual contractual arrangements had been entered into and that this plan was on the basis of a gentlemen's agreement. It was pointed out that in Kansas there was no organization comparable to the Massachusetts Medical Service (Blue Shield).

In reply to a question, Dr McCarthy said that the contract that the physician participating in Blue Shield enters into concerns the administration of surgical and obstetric services only. He explained that this was not an all-inclusive contract and that the contract signed by the Blue Shield and the Veterans Administration would be all inclusive from the standpoint of the services offered. He added that the fee schedule now in force under the Blue Shield had nothing to do with the plan proposed.

In reply to a question, Dr Norman A Welch, Norfolk, said that the Blue Shield is open to any licensed practitioner of medicine in Massachusetts.

The motion was adopted by vote of the Council.

Dr Reardon moved that the final approval of any contract entered into with the Veterans Administration concerning the Massachusetts Medical Society be delegated to the Executive Committee of the Council. This motion was seconded.

It was explained by the Secretary that the Executive Committee was in approval of this motion, whose intent was to make it unnecessary to call the Council together for the sole purpose of formally approving a contract that would be based on the agreements reached at this meeting of the Council.

The motion was adopted by vote of the Council.

Dr Leavitt moved that when the contract heretofore referred to was under consideration in Washington, there should be on hand one or more duly appointed representatives of the Society empowered to approve any minor changes in the fee schedule that might prove advantageous. This motion was seconded by Dr Alexander J A Campbell, Suffolk.

Dr Albert A. Hornor, Suffolk, moved as an amendment to the motion the deletion of the words "in Washington." This amendment was seconded by Dr Dwight O'Hara, Middlesex South. The motion as amended was adopted by vote of the Council.

The Secretary, speaking for the Executive Committee, made the following recommendation:

Certain questions arose in the committee that had to do with circumstances that concern the payment of the physician giving the prenatal and postnatal care, but not delivering the case. This same type of discussion arose in connection with the preoperative and postoperative service rendered by the physician who did not perform the operation involved. This discussion also concerned itself with the fees that should be allowed the surgeon's assistant at operations.

- 57 Collins, E. T. Pseudoglioma *Royal Lond Ophth Hosp Rep* 13 361-394, 1892
- 58 Pollack, W. B. I. Case of pseudo-gloma due to persistence and thickening of posterior fibrovascular sheath of lens *Tr Ophth Soc U K* 43 263-272, 1923
- 59 Parsons, J. H. Microscopical section of pseudo-gloma, due to congenital membrane behind lens *Tr Ophth Soc U K* 22 253, 1902
- 60 Gifford, S. R., and Latta, J. S. Pseudoglioma and remains of tunica vasculosa lentis *Am J Ophth* 6 565-571, 1923

- 61 Lloyd, R. I. Pseudoglioma, with special reference to type associated with remains of tunica vasculosa lentis. *Am J Ophth* 14 2733, 1931
- 62 Clifford, S. Personal communication to Dr T. L. Terry
- 63 Mann, I. *Developmental Anomalies of the Eye* 444 pp London Cambridge University Press, 1937
- 64 Haden, H. C. Concerning certain phases of development of vitreous demonstration of lantern slides *Tr Am Ophth Soc* 39 41-48, 1941
- 65 Gregg, M. N. Congenital cataract following German measles in mother *Tr Ophth Soc Australia* 3 35-46 1942

MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Special Meeting, April 10, 1946

THE Council of the Massachusetts Medical Society met in special session on Wednesday, April 10, 1946, in Building E, Harvard Medical School, Longwood Avenue, Boston. The meeting was called to order by the president, Dr Reginald Fitz, at 10 30 a m. Dr Michael A. Tighe served as secretary. One hundred and forty-four councilors were present (Appendix 1).

In opening the meeting Dr Fitz stated that the Council had not met in Harvard Medical School since 1825. He added that before that date it had met in this school several times. He said that this gave a certain historic interest to the meeting.

He introduced Dr C. Sidney Burwell, dean of Harvard Medical School, who spoke of the close relation that existed between the Massachusetts Medical Society and Harvard Medical School in the infancy of both and who added that, in their maturity, they were still not very far apart. Dr Burwell graciously welcomed the councilors and asked them to come again.

The business before this meeting was the report of a special committee, which had been appointed to confer with Major General Hawley, medical director of the Veterans Administration, concerning the medical care of veterans by civilian physicians.

The report of this committee presented by Dr Humphrey L. McCarthy, Norfolk, chairman, as amended by the Council, is as follows:

On February 6, 1946, the appointment of the Special Committee on Veterans' Care, comprising J. J. Dunphy, Worcester, H. L. McCarthy, Norfolk, and M. A. Tighe, Middlesex North, was formally confirmed by vote of the Council. This committee had been appointed in January by the President as a matter of emergency and at the request of Major General P. R. Hawley, of the Veterans Administration in Washington, who asked for a committee from the Society to confer with him about the medical care of veterans in Massachusetts.

Throughout its work, this committee has steadfastly borne in mind the Council's belief that the most satisfactory and economical care of veterans in Massachusetts could be obtained by granting them free choice of physicians in their own communities, this service to be paid for at prevailing rates, and, if hospitalization were required, by granting them hospitalization privileges in local licensed hospitals of their own choice.

Here is reported the committee's actions:

On January 14, 1946, the committee went to Washington to meet with General Hawley's representative. We were informed that the Veterans Administration favored

the local care of veterans along the lines approved by the Council. Up to that time, two types of contract to meet this general aim had been established, one with the Michigan Medical Service and another with the Kansas Medical Society.

Under the Michigan plan, doctors affiliated with the Michigan Medical Service who wished to take care of veterans were to be paid according to an agreed fee schedule through the Michigan Medical Service, which in turn was to be paid by the Veterans Administration. The Michigan Medical Service was to collect the amount to be paid for professional care plus 7 per cent, the latter sum representing the estimated costs necessary to the administration of such a plan.

The Kansas plan entailed the Society's submitting a list of its members who desired to work for the Veterans Administration under an established fee schedule. The society was to zone the state in an appropriate manner, offices of the Veterans Administration were to be established where needed and were to administer the plan directly.

Under either plan, a fee schedule was required. Therefore, the committee was informed that a fee schedule acceptable to participating doctors in Massachusetts was the first step in the development of any plan for veterans' care in this region outside that offered in veterans' hospitals.

We have constructed a fee schedule, which has been built up as fairly as possible, and in our judgment represents an honest appraisal of charges prevailing among Massachusetts practitioners for the services listed. The figures were obtained by consultation with individual physicians, with groups of physicians in different parts of the Commonwealth, and from representatives of the various specialty boards and special societies who happen to be residents of the Commonwealth.

We recommend the adoption by the Massachusetts Medical Society of this fee schedule as the first step in the activation of a plan for offering Massachusetts veterans optimum medical care by civilian physicians and in civilian hospitals.

We were given to understand that contractual arrangements might be established between the Veterans Administration and the Blue Cross-Blue Shield, whereby the hospital expenses of veterans in civilian hospitals would be met by the Blue Cross as agent and whereby the costs of professional services of civilian physicians caring for veterans under the fee schedule would be met by the Blue Shield as agent.

We believe that this plan is preferable to the Kansas plan and recommend its adoption. We have consulted with both the Blue Cross and the Blue Shield and have been informed that they are willing to undertake its administration. The Blue Shield agrees that an 8 per cent charge for expenses of administration is reasonable.

Should the Council adopt the plan thus outlined, we believe that the next step is for our attorneys and the attorneys of the Blue Cross and the Blue Shield to frame a contract acceptable to the three organizations involved. We recommend that final approval of any such contract as it concerns the Massachusetts Medical Society should be delegated to the Executive Committee.

Such a contract in its final form should then be presented to the proper authorities. It would represent the

e Surgery

- (1) Biopsy, not including cost of histologic section, culture and clinical examination
 - (a) Superficial 5 40
 - (b) Lymph node 10 80
 - (c) Needle aspiration 5 40
- (2) Acne 5 40
- (3) Incising localized abscess, boil, etc 5 40
- (4) Excising
 - (a) Benign lesions, uncomplicated (cyst, mole, fibroma, verruca, keratosis, etc) 10 80
 - (b) Benign lesions, complicated 16 20
 - (c) Nails (ingrown or infected, or both) radical removal 16 20
 - (d) Malignant lesions 27 00

f Injections

- (1) Routine (calcium, sodium thiosulfate, etc) 5 40
- (2) Special
 - (a) Gold sodium thiosulfate 5 40
 - (b) Estrogens 5 40
 - (c) Vaccines 5 40
 - (d) Other parenteral injections (serums, liver, vitamin, venom, etc) 5 40
 - (e) Sclerosing (hemangioma, etc) 10 80

g Ultraviolet radiation

- (1) Alpine lamp 5 40
- (2) Kromayer lamp 5 40
- (3) Wood's filter examination 5 40

h Carbon dioxide snow (topical application)

- (1) 10 80

i Fulguration

- (1) Benign lesions 10 80
- (2) Malignant lesions 16 20

j X-ray therapy

- (1) Localized area 10 80
- (2) Generalized (spray) 10 80
- (3) Plantar wart 10 80
- (4) Spinal sympathectomy 10 80
- (5) Epilation
 - (a) Scalp (favus infection, etc.) 27 00
 - (b) Beard (tinea barbae, etc) 27 00

k Radium

- (1) 25 millicurie hours or less 21 60
- (2) 26 to 100 millicurie hours 43 20
- (3) 101 to 500 millicurie hours 81 00
- (4) 50 millicurie hours or more 135 00

l Electrolysis

- (1) Mole 27 00
- (2) Face (half-hour) 10 80

m Antiohemotherapy

- (1) 10 80

n Syphilis

- (1) Darkfield (open lesion) 10 80
- (2) Lymph-node puncture and darkfield 21 60
- (3) Arsenical treatment, intravenous 10 80
- (4) Bismuth treatment, intramuscular 5 40
- (5) Follow-up (5-6-9-12 months, 2, 3, 4, 5, years) serology, urine and examination (per visit) 10 80
- (6) All penicillin injections (massive doses) 10 80

o Granuloma inguinale

- (1) Biopsy plus cost histologic section 16 20
- (2) Treatment
 - (a) Intravenous 10 80
 - (b) Intramuscular 5 40
 - (c) Surgical excision 27 00

p Lymphopathia venereum

- (1) Frei test 10 80
- (2) Reading Frei test 5 40
- (3) Biopsy (plus cost histologic section) 16 20
- (4) Treatment
 - (a) Intravenous 10 80
 - (b) Intradermal 5 40
 - (c) Intramuscular 5 40
 - (d) X-ray (per treatment) 10 80
 - (e) Surgical excision 16 20
 - (f) Incision and drainage 16 20

q Patch tests

- (1) Initial visit 5 40
- (2) Subsequent visits 5 40

r Immunologic tests (intradermal and scratch)

- (1) 27 00

2 Home

a Consultation (see Internal Medicine)

b Radium

- (1) 25 millicurie hours or less 27 00
- (2) 26 to 100 millicurie hours 49 00
- (3) 101 to 500 millicurie hours 86 40
- (4) 501 millicurie hours or more 139 40
- (5) Travel over 10 miles (per mile) 1 08

c Antiohemotherapy

- (1) 10 80

d Injections

- (1) Intravenous 10 80
- (2) Intramuscular or intradermal 10 80

Internal Medicine (including allergy, arthritis, cardiology, communicable diseases, diabetes, endocrinology, gastroenterology, hematology, nutritional dietetics, parasitology and tuberculosis)

1 Consultations

a Office (to include routine urines, bloods and sputum examinations as indicated and the simpler blood chemical tests and electrocardiogram)

- (1) Initial visit 21 60
- (2) Subsequent visits 5 40

b Outside office (to include routine urines, bloods and sputum examinations as indicated and the simpler blood chemical tests and electrocardiogram)

- (1) Within 10-mile radius 27 00
- (2) Outside 10-mile radius (per mile) 1 08
- (3) Additional patients seen at same visit (per patient) 21 60

c Patient cared for by the consultant in hospital shall be charged for the first week (per day)

- Except in emergencies, such as diabetic coma, acute bulbar poliomyelitis or laryngeal diphtheria, requiring constant attendance, in case the fee would be — per hour 10 80
- May be charged up to a maximum of 54 00
- After the first week charge shall be — per week 27 00

2 Miscellaneous

- a First aid 5 40
- b Report of former medical examination — for six pages — or less 5 40
- for each additional page 54

3 Local Physician

a Home visits

- (1) 8-00 a m to 8-00 p m
 - (a) Within 3 miles 5 40
 - (b) Over 3 miles (add per mile) 81
- (2) 8-00 p m to 8-00 a m
 - (a) Within 3 miles 10 80
 - (b) Over 3 miles (add per mile) 81

b Office visits

- (1) 4 32

Pediatrics

1 During first month of life office

- a Initial visit 10 80
- b Subsequent visits (per visit) 5 40
- (maximum \$27 per week, exclusive of original visit)

2 During first year of life fee-for-service office basis

- a Periodic physical examinations and regulation of diet, not more frequent than every 4 weeks (per visit) 5 40
- b Complete 3 inoculations whooping-cough immunization* 6 48
- c Complete 3 inoculations diphtheria immunization* 6 48
- d Smallpox vaccination, up to three attempts for each child (per vaccination)* 3 24

3 During first year of life flat-fee office basis (to include immunization against smallpox, diphtheria, tetanus and whooping cough,* a minimum of six complete physical examinations spaced during the first year, office treatment of minor conditions, instruction of the

*The charges for inoculations referred to in these schedules do not include the cost of material used

It was thought that \$54.00 should be allowed for the physician giving the prenatal and postnatal care, and that in simple cases \$54.00 should be allowed for the physician delivering the case. In difficult cases, a consultant delivering the case should receive a fee of \$75.00. In this discussion it came out that this division of fees represents an administrative detail that should not appear in the schedule but should go, as a recommendation, to the administrative agent, which, in this case, it is hoped will be the Blue Shield.

The Secretary moved the adoption of this recommendation. This motion was seconded and it was so ordered by vote of the Council.

The Secretary continued:

The Executive Committee being conscious that such administrative problems may be numerous, at least during the early days of the administration of this plan by the Blue Shield, offers the following recommendation:

That a special committee of five be appointed by the President, and that this committee, representing the Massachusetts Medical Society, be empowered to act in an advisory capacity to the Blue Shield in the interpretation of the Veterans' Fee Schedule.

The Secretary moved the adoption of this recommendation. This motion was seconded by Dr. Leavitt, and it was so ordered by vote of the Council.

Dr. Leavitt moved the adoption of the report as a whole and as amended. This motion was seconded by Dr. Reardon, and it was so ordered by vote of the Council.

At the suggestion of the President, the Council extended a rising vote of thanks to the members of the committee who so devotedly put this report together.

It was moved and seconded that the Council adjourn. This motion was adopted by vote of the Council.

The President declared the Council adjourned at 6:30 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE OF COUNCILORS

BRISTOL NORTH	C. F. Twomey
R. M. Chambers	C. A. Worthen
W. J. Morse	
J. L. Murphy	FRANKLIN
	J. E. Moran
BRISTOL SOUTH	HAMPDEN
G. W. Blood	E. P. Bagg
R. B. Butler	J. L. Chereskin
E. D. Gardner	E. C. Dubois
C. C. Tripp	Frederic Hagler
ESSEX NORTH	G. D. Henderson
E. S. Bagnall	Charles Jurist
G. J. Connor	A. H. Riordan
H. R. Kurth	J. A. Seaman
P. J. Look	
G. L. Richardson	MIDDLESEX EAST
F. W. Snow	J. L. Anderson
C. F. Warren	Richard Dutton
ESSEX SOUTH	E. M. Halligan
Bernard Appel	MIDDLESEX NORTH
R. E. Foss	J. J. Cassidy
P. P. Johnson	A. R. Gardner
E. D. Reynolds	M. A. Tighe
P. E. Tivnan	

MIDDLESEX SOUTH

E. W. Barron
J. D. Bepnett
G. F. H. Bowers
Madeline R. Brown
R. N. Brown
R. W. Buck
E. J. Butler
C. W. Clark
J. A. Daley
C. L. Derick
J. G. Downing
C. W. Finnerty
H. G. Giddings
J. L. Golden
A. D. Guthrie
Eliot Hubbard, Jr.
A. M. Jackson
A. A. Levi
A. N. Makechnie
C. E. Mongan
G. M. Morrison
J. P. Nelligan
Dwight O'Hara
E. H. Robbins
M. J. Schlesinger
E. W. Small
J. E. Vance
C. F. Walcott
A. L. Watkins
Hovhannes Zovickian

NORFOLK

C. E. Allard
B. E. Barton
Carl Bearse
M. I. Berman
D. J. Collins
G. L. Doherty
Albert Ehrenfried
H. M. Emmons
Susannah Friedman
R. J. Heffernan
P. J. Jakmauh
I. R. Jankelson
C. J. Kickham
D. S. Luce
C. M. Lydon
F. P. McCarthy
H. L. McCarthy
F. J. Moran
Hyman Morrison
D. J. Mullane
J. J. O'Connell
W. R. Ohler
S. A. Robins
D. D. Scannell
L. A. Sieracki
Kathleyne S. Snow
S. L. Skvirsky
J. W. Spellman

W. J. Walton
N. A. Welch

NORFOLK SOUTH

C. S. Adams
D. L. Belding
Harry Braverman
Frederick Hinchliffe
D. B. Reardon

PLYMOUTH

A. L. Duncombe
P. B. Kelly
P. H. Leavitt
B. H. Peirce

SUFFOLK

A. J. A. Campbell
Reginald Fitz
Maurice Fremont-Smith
R. L. Goodale
A. A. Horner
L. M. Hurxthal
H. A. Kelly
C. C. Lund
H. L. Musgrave
H. F. Newton
R. N. Nye
F. W. O'Brien
Helen S. Pittman
J. H. Pratt
H. F. Root
M. C. Sosman
S. N. Vose
Conrad Wesselhoeft

WORCESTER

C. R. Abbott
A. W. Atwood
Gordon Berry
F. P. Bousquet
E. J. Crane
J. M. Fallon
J. V. Gallagher
L. P. Leland
W. F. Lynch
J. C. McCann
A. E. O'Connell
H. L. Paine
R. S. Perkins
O. H. Stansfield
R. J. Ward
B. C. Wheeler

WORCESTER NORTH

H. C. Arey
D. B. Cheatham
C. B. Gay
J. V. McHugh
J. G. Simmons

APPENDIX NO. 2

FEE SCHEDULE APPROVED BY THE COUNCIL OF THE MASSACHUSETTS MEDICAL SOCIETY FOR MEDICAL SERVICES RENDERED UNDER THE VETERANS ADMINISTRATION MEDICAL CARE PROGRAM

Dermatology (including syphilis, granuloma inguinale and lymphopathia venereum)

1. Office	
a. Consultation	\$16.20
b. Visit	
(1) Initial (history, examination and prescribing)	10.80
(2) Subsequent prescribing	5.40
c. Dressings	5.40
d. Unna boot	10.80

for anesthesia supervision of premedication, selection of anesthetic agents and methods, the administration of anesthetic agents, the treatment of all complications pertaining to anesthesia during the operation and postoperatively and the treatment of certain medical conditions, such as pulmonary and other conditions requiring the services of an anesthesiologist — i.e. asphyxia, drug poisoning, caisson disease, asthma, convulsions, etc.)

a Inhalation anesthesia

- (1) Ether — up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40

(2) Gas

(a) Conventional

- (1) Nitrous oxide up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(2) Ethylene, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(3) Carbon dioxide, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(4) Oxygen, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40

(b) Special

- (1) Cyclopropane, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(2) Helium and oxygen up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(3) Venethene, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(4) Ethyl chloride, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(5) Chloroform, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(6) Curare 16 20

b Regional anesthesia

- (1) Spinal
(a) With or without supplement, up to $\frac{1}{2}$ hr 16 20
Each additional $\frac{1}{2}$ hour 5 40
(b) Continuous, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(2) Local infiltration, with or without supplement, up to $\frac{1}{2}$ hour 16 20
(3) Nerve block, with or without supplement
(a) Minor (single nerve), up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(b) Major
(a) (Paravertebral) up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(b) Plexus, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(4) Field block, with or without supplement, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(5) Topical (permeation), up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40

c Intravenous anesthesia, with or without supplement

- (1) Pentothal Sodium, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(2) Sodium Evipal, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40

d Rectal anesthesia, with or without supplement

- (1) Tribromethanol in amylene hydrate (Avertin, fluid), up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(2) Paraldehyde, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40
(3) Evipal Soluble, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(4) Pentothal, up to $\frac{1}{2}$ hour 16 20
Each additional $\frac{1}{2}$ hour 5 40
(5) Ether-in-oil, up to $\frac{1}{2}$ hour 10 80
Each additional $\frac{1}{2}$ hour 5 40

e. Special techniques

- (1) Intratracheal anesthesia — up to $\frac{1}{2}$ hour (additional) 5 40
(2) Suction bronchoscopy 16 20
(3) Venoclysis 5 40

- (4) Transfusions 21 60
(5) Refrigeration 16 20

2 Chemical Pathology

a Bacteriological

- (1) Cultural examination for fungi 5 40
(2) Routine culture 2 16
(3) Pus or exudate, cultural examination, including classification of organism 5 40
(4) Throat culture, including classification of organism 5 40
(5) Blood culture 5 40
(6) Examination of smears 2 16

b Pathological

- (1) Autopsy 54 00
(2) Tissue examination, including smear for carcinoma 5 40
(3) Frozen section (rush diagnosis at laboratory) 10 80
(4) Frozen section (rush diagnosis at hospital) 27 00
(5) Guinea-pig inoculation 5 40

c Blood

- (1) Red count, white count, differential and hemoglobin 5 40
(2) Red count 2 16
(3) White count 2 16
(4) Differential 2 16
(5) Hemoglobin (Sahli) 2 16
(6) Platelet count 2 16
(7) Malarial parasites 5 40
(8) Bleeding and coagulation times 2 16
(9) Fragility test 5 40
(10) Sedimentation time 5 40
(11) Clot retraction 2 16
(12) Prothrombin time 3 24
(13) Hematocrit 5 40
(14) Grouping for transfusion 3 24
(15) Direct agglutination 5 40
(16) Aschheim-Zondek test 10 80
(17) Kahn test 3 24
(18) Hinton test (routine) 3 24
(19) Hinton test (rapid) 3 24
(20) Kolmer-Wassermann test 5 40
(21) Schwartz-McNeil test (complement-fixation test for gonorrhea) 5 40
(22) Heterophile antibody reaction 3 24
(23) Rh factor 5 40

d Blood chemistry

- (1) Albumin-globulin ratio 10 80
(2) Bromide 3 24
(3) Calcium 5 40
(4) Cephalin-cholesterol 3 24
(5) Chloride 3 24
(6) Cholesterol 6 48
(7) Carbon dioxide combining power 5 40
(8) Creatine 3 24
(9) Diastase 3 24
(10) Galactose-tolerance test 5 40
(11) Icterus index 2 16
(12) Nonprotein nitrogen 3 24
(13) Phosphatase, acid 5 40
(14) Phosphatase, alkaline 5 40
(15) Phosphorus 5 40
(16) Potassium thiocyanate 3 24
(17) Sugar 3 24
(18) Sugar and nonprotein nitrogen (same blood) 5 40
(19) Sulfonamide, concentrations 3 24
(20) Total protein 3 24
(21) Urea nitrogen 3 24
(22) Uric acid 3 24
(23) Van den Bergh 5 40

e Feces

- (1) Gross and microscopic (complete) 5 40
(2) Occult blood 2 16
(3) Fat 1 08
(4) Parasites 5 40

f Skin tests

- (1) Protein tests (each group of 25 proteins) 5 40
(2) Hay-fever test 5 40

mother in infant care and supervision of infant feeding)			b Myelography	37 80
		70 20	c Pelvis	10 80
4	Routine care after first year (periodic health examinations, maximum two per year) (per visit)	5 54	d All stereoscopic spine or pelvis (for each part)	5 54
5	Care of sick infant or child		4 Upper extremities	
a	At home		a Shoulder girdle	10 80
(1)	Per visit		b Clavicle	10 80
(a)	Day	5 40	c Shoulder joint	10 80
(b)	Night	10 20	d Humerus (shaft)	10 80
(2)	Maximum for any 3-week period	108 00	e Elbow	10 80
b	At hospital		f Forearm	10 80
(1)	Per visit	5 40	g Wrist	10 80
(2)	Maximum for any 3-week period	108 00	h Hand	10 80
6	Consultations		i Finger	5 40
	Office (maximum)	16 20	j Stereoscopic studies (extra)	5 40
	Hospital — when consultant is on staff (maximum)	16 20	5 Lower extremities	
	Home or hospital when consultant is not on staff	27 00	a Hip	10 80
<i>Psychiatry</i>			b Femur	10 80
1	Consultations		c Knee	10 80
a	Office		d Tibia and fibula	10 80
(1)	Initial visit	21 60	e Ankle	10 80
(2)	Subsequent visits (per visit)	10 80	f Foot	10 80
(b)	House or hospital		g Toes	5 40
(1)	Within 10 miles	27 00	h Injection of sinuses for chronic osteomyelitis	21 60
(2)	Beyond 10 miles (add per mile)	1 08	i Stereoscopic studies (extra)	5 40
2	Special procedures		6 Gastrointestinal tract	
(a)	Shock treatment O P D (includes assistant's fee)	27 00	a Barium meal, with or without preliminary film of abdomen	21 60
(b)	Electroencephalogram (standard fee)	10 80	b Barium meal and enema	32 40
(c)	Pneumoencephalogram (exclusive of x-ray films)	54 00	c Barium meal, gall bladder (dye) and enema	37 80
<i>Röntgenology</i>			d Stomach and duodenum (check up)	16 20
1	Head and neck		e Stomach, duodenum and gall bladder (dye)	32 40
a	Skull, lateral stereoscopic and anteroposterior and posteroanterior stereoscopic	16 20	f Gall bladder and dye method	16 30
b	Skull, including paranasal sinuses	21 60	g Fistula (contrast study)	21 60
c	Paranasal sinuses	16 20	h Colon by barium enema (complete)	21 60
d	Encephalography, including preliminary skull	27 00	(1) Followed by air-contrast enema	27 00
e	Ventriculography, including preliminary skull	27 00	i Colon and gall bladder (dye)	27 00
f	Eye for foreign body	10 80	j Special small-bowel study	21 60
(1)	For localizing foreign body (extra)	16 20	k Cholangiogram	21 60
g	Mastoids, regular, including petrous pyramids	10 80	l Kidney in situ (operation table)	10 80
h	Nose	10 80	7 Urinary tract	
i	Maxilla and facial bones	10 80	a Simple K U B	10 80
j	Mandibles (each)	10 80	b Pyelography	27 00
k	Esophagus, including fluoroscopy	16 20	(1) Intravenous (injection of dye)	16 20
l	Sialography (without medium)	10 80	(2) Retrograde (x-ray only)	16 20
m	Optic foramina	10 80	c Cystography	16 20
n	Neck, for soft tissue (anteroposterior and lateral)	10 80	d Urethrocytography	16 20
o	Teeth (complete set)	16 20	8 Genital tract	
2	Chest		a Pregnancy	16 20
a	Thorax (ribs)	10 80	(1) With measurements	10 80
b	Sternum	10 80	(2) Without measurements	10 80
c	Lungs (stereoscopic, anteroposterior and lateral)	16 20	b Uterosalpingography (with injection of medium)	21 60
(1)	Fluoroscopic examination (alone)	5 40	9 Fluoroscopic (to include reduction of fractures, foreign-body detection, foreign-body removal and foreign bodies in esophagus or respiratory tract)	21 60
d	Heart, complete fluoroscopic and radiographic studies	16 20	10 General	
(1)	Single teleroentgenogram	10 80	a Mammary-gland study	16 20
e	Bronchography (with medium instillation)	37 80	(1) With air injection	27 00
3	Spine and pelvis		b Interpretation of films	5 40
a	Spine		c Portable	27 00
(1)	Cervical	10 80	(1) Within 10 miles	1 08
(2)	Thoracic	10 80	(2) Beyond 10 miles (add per mile)	
(3)	Lumbar	10 80	11 Therapy	
(4)	Lumbar and pelvis	16 20	a X-ray treatments	
(5)	Coccyx and sacrum	16 20	(1) Each	10 80
(6)	Any two of the above areas	21 60	(2) Series (maximum)	108 00
(7)	Entire without cervical spine	27 00	b Radium treatments	
(8)	Entire with cervical spine		(1) 25 millicurie hours or less	27 00
			(2) 26 to 100 millicurie hours	49 00
			(3) 101 to 500 millicurie hours	86 40
			(4) 501 millicurie hours or more	139 40
			(5) Travel over 10 miles (add per mile)	1 08
			(6) Follow-up examination (each)	5 40
<i>Surgery</i>			1 Anesthesia (the practice of anesthesiology includes the preliminary preparation of the patient	

for anesthesia, supervision of premedication, selection of anesthetic agents and methods, the administration of anesthetic agents, the treatment of all complications pertaining to anesthesia during the operation and postoperatively and the treatment of certain medical conditions, such as pulmonary and other conditions requiring the services of an anesthesiologist — i.e. asphyxia, drug poisoning, caisson disease, asthma, convulsions, etc.)

a Inhalation anesthesia

(1) Ether — up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(2) Gas	
(a) Conventional	
(1) Nitrous oxide up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(2) Ethylene, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(3) Carbon dioxide, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(4) Oxygen, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(b) Special	
(1) Cyclopropane, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(2) Helium and oxygen, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(3) Venethene, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(4) Ethyl chloride, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(5) Chloroform up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(6) Curare	16 20

b Regional anesthesia

(1) Spinal	
(a) With or without supplement, up to $\frac{1}{2}$ hr	16 20
Each additional $\frac{1}{2}$ hour	5 40
(b) Continuous, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(2) Local infiltration, with or without supplement, up to $\frac{1}{2}$ hour	16 20
(3) Nerve block, with or without supplement	
(a) Minor (single nerve), up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(b) Major	
(a) (Paravertebral) up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(b) Plexus, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(4) Field block, with or without supplement, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(5) Topical (permeation), up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40

c Intravenous anesthesia, with or without supplement

(1) Pentothal Sodium, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(2) Sodium Evipal, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40

d Rectal anesthesia, with or without supplement

(1) Tribromethanol in amylene hydrate (Avertin, fluid), up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(2) Paraldehyde, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40
(3) Evipal Soluble, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(4) Pentothal, up to $\frac{1}{2}$ hour	16 20
Each additional $\frac{1}{2}$ hour	5 40
(5) Ether-in-oil, up to $\frac{1}{2}$ hour	10 80
Each additional $\frac{1}{2}$ hour	5 40

e Special techniques

(1) Intratracheal anesthesia — up to $\frac{1}{2}$ hour (additional)	5 40
(2) Suction bronchoscopy	16 20
(3) Venoclysis	5 40

(4) Transfusions	21 60
(5) Refrigeration	16 20

2 Clinical Pathology

a Bacteriological

(1) Cultural examination for fungi	5 40
(2) Routine culture	2 16
(3) Pus or exudate, cultural examination, including classification of organism	5 40
(4) Throat culture, including classification of organism	5 40
(5) Blood culture	5 40
(6) Examination of smears	2 16

b Pathological

(1) Autopsy	54 00
(2) Tissue examination, including smear for carcinoma	5 40
(3) Frozen section (rush diagnosis at laboratory)	10 80
(4) Frozen section (rush diagnosis at hospital)	27 00
(5) Guinea-pig inoculation	5 40

c Blood

(1) Red count, white count, differential and hemoglobin	5 40
(2) Red count	2 16
(3) White count	2 16
(4) Differential	2 16
(5) Hemoglobin (Sahl)	2 16
(6) Platelet count	2 16
(7) Malarial parasites	5 40
(8) Bleeding and coagulation times	2 16
(9) Fragility test	5 40
(10) Sedimentation time	5 40
(11) Clot retraction	2 16
(12) Prothrombin time	3 24
(13) Hematocrit	5 40
(14) Grouping for transfusion	3 24
(15) Direct agglutination	5 40
(16) Aschheim-Zondek test	10 80
(17) Kahn test	3 24
(18) Hinton test (routine)	3 24
(19) Hinton test (rapid)	3 24
(20) Kolmer-Wassermann test	5 40
(21) Schwartz-McNeil test (complement-fixation test for gonorrhea)	5 40
(22) Heterophile antibody reaction	3 24
(23) Rh factor	5 40

d Blood chemistry

(1) Albumin-globulin ratio	10 80
(2) Bromide	3 24
(3) Calcium	5 40
(4) Cephalin-cholesterol	3 24
(5) Chloride	3 24
(6) Cholesterol	6 48
(7) Carbon dioxide combining power	5 40
(8) Creatine	3 24
(9) Diastase	3 24
(10) Galactose-tolerance test	5 40
(11) Icterus index	2 16
(12) Nonprotein nitrogen	3 24
(13) Phosphatase, acid	5 40
(14) Phosphatase, alkaline	5 40
(15) Phosphorus	5 40
(16) Potassium thiocyanate	3 24
(17) Sugar	3 24
(18) Sugar and nonprotein nitrogen (same blood)	5 40
(19) Sulfonamide, concentrations	3 24
(20) Total protein	3 24
(21) Urea nitrogen	3 24
(22) Uric acid	3 24
(23) Van den Bergh	5 40

e Feces

(1) Cross and microscopic (complete)	5 40
(2) Occult blood	2 16
(3) Fat	1 08
(4) Parasites	5 40

f Skin tests

(1) Protein tests (each group of 25 proteins)	5 40
(2) Hay-fever test	5 40

g Spinal fluid			(2) Simple excision, with plastic	81 00
(1) Complete	27 00		(3) Excision, with upper-neck dissection	81 00
(2) Cell count	2 70			
(3) Culture	2 16	c	Radical dissection of neck (one side)	108 00
(4) Quantitative		d	Carcinoma of tongue, excision	108 00
(a) Protein	8 10	e	Implantation of radium, tongue	108 00
(b) Sugar	5 40	f	Excision	
(c) Chloride	5 40		(1) Thyroglossal cyst or sinus	108 00
(5) Gold-sol test	5 40		(2) Branchial cyst	108 00
(6) Davies-Hinton test	3 24		(3) Submaxillary gland	81 00
(7) Kolmer-Wassermann test	5 40		(4) Mixed tumor parotid	108 00
h Stomach contents			(5) Malignant tumor parotid	162 00
(1) Gastric analysis	5 40		(6) Esophageal diverticulum, two stages	216 00
i Urine		g	Biopsy	
(1) Routine (complete)	2 16		(1) Lymph nodes of neck	27 00
(2) Routine, without microscopic	1 08		(2) Tumor of neck (deep)	54 00
(3) Microscopic alone	1 08	h	Incision and drainage	
(4) Hippuric acid	3 24		(1) Superficial cervical abscess	27 00
(5) Diastase	3 78		(2) Deep cervical abscess	54 00
(6) Urobilinogen	2 16		(3) Submental abscess	27 00
(7) Kidney-function test (phenolsulfone-phthalein)	3 24		(4) Ludwig's angina	162 00
(8) Bence-Jones protein	3 24		(5) Ludwig's angina, with tracheotomy	162 00
(9) Aschheim-Zondek test	10 80	i	Dilatation of esophagus	54 00
j Miscellaneous		j	Excision of thyroid adenoma	108 00
(1) Basal-metabolism test	5 40	k	Thyroidectomy	
(2) Autogenous vaccine	10 80		(1) Total	216 00
(3) Hormone studies (by arrangement)			(2) Subtotal (two stages)	189 00
(4) Glucose-tolerance test (including determination of blood and urine sugar)	10 80		(3) Subtotal (one stage)	135 00
3 Diabetic Surgery		l	Carcinoma of thyroid	
a Infections of skin and subcutaneous tissues, excluding carbuncles			(1) Removal of one lobe, with neck dissection	189 00
(1) Incision and drainage, including one week's postoperative dressings	54 00	m	(2) Removal of isthmus	108 00
(2) Subsequent hospital care		n	Incision and drainage, thyroiditis	108 00
(a) Per week	27 00	o	Exploration and biopsy, thyroid	216 00
(b) Maximum	162 00	p	Removal of parathyroid adenoma	216 00
b Carbuncles		q	Transpleural resection of esophagus	
(1) Incision and drainage or excision, including one week's postoperative dressings	81 00		Transpleural resection of stomach, partial or total	216 00
(2) Subsequent hospital care		r	Gastrectomy, abdominal	216 00
(a) Per week	27 00		(1) Complete	
(b) Maximum	270 00		(2) Subtotal, with or without excision of ulcer	189 00
(3) Excision and skin graft	108 00	s	Gastrosctomy	54 00
c Upper extremities		t	Gastroscopy	135 00
(1) Amputations — infections of hand (charge for operation same as in patient without diabetes)		u	Gastrostomy	162 00
(a) Postoperative dressings		v	Gastroenterostomy, anterior or posterior	162 00
(r) Per week	27 00	w	Pyloroplasty	135 00
(2) Maximum	270 00	x	Perforated peptic ulcer, closure	189 00
d Lower extremities		y	Gastrojejunal ulcer	270 00
(1) Infection and gangrene		z	Gastrojejunal colic fistula (two stages)	
(a) Amputation			Acute pancreatitis	
(r) Through or above lower leg	135 00		(1) Drainage of pancreas	108 00
(2) Secondary closure or reamputation	243 00		(2) Drainage of pancreas and gall bladder	135 00
(3) One or more digits (open or closed) through a phalanx	54 00		(3) Drainage of pancreas and common duct	162 00
(b) Incision and drainage		aa	Carcinoma of pancreas, radical	
(r) Superficial infection of foot, including one week's aftercare	54 00		(1) One stage	216 00
(a) Subsequent surgical care (per week)	27 00		(2) Two stages	270 00
(b) Maximum	162 00	bb	Carcinoma of extrahepatic biliary tree	216 00
(2) Deep infection of foot, with or without the amputation of one or more toes, including one week's aftercare	108 00	cc	Exploratory laparotomy	108 00
(a) Subsequent surgical care per week	27 00	dd	Lysis of adhesions	108 00
(b) Maximum	270 00	ee	Pyloric stenosis (Rammstedt's operation)	162 00
(c) Multiple operations on an extremity during same hospital admission, including aftercare — maximum	270 00	ff	Cholecystostomy	108 00
4 General Surgery		gg	Cholecystectomy	162 00
a Consultations (see Internal Medicine)		hh	Cholecystostomy or cholecystectomy, with exploration common duct	189 00
b Carcinoma of lip (upper or lower)		ii	Plastic procedures on common duct	216 00
(1) Simple excision	54 00	jj	Re-exploration of common duct	216 00
		kk	Cholecystenterostomy	162 00
		ll	Cholecystoduodenostomy	162 00
		mm	Cholecystgastrostomy	162 00
		nn	Splenectomy	162 00
		oo	Intussusception, with simple reduction	135 00
		pp	Volvulus, with reduction	135 00
		qq	Appendectomy	
			(1) Uncomplicated	108 00
			(2) Ruptured	135 00

	(3) Secondary (following abscess or peritonitis)	135 00	aaaa	Lumbar sympathetic block	27 00
rr	Resection of bowel	216 00	bbbb	Cervicodorsal sympathetic block	37 00
ss	Cecostomy	108 00	cccc	Arteriovenous aneurysm, quadruple ligation	216 00
tt	Colostomy, temporary or permanent	108 00	dddd	Arterial aneurysmorrhaphy	270 00
uu	Mikulicz's resection, including crushing of spur and first closure	270 00	eeee	Arterial femoral embolectomy, with sympathetic block	135 00
vv	Miles's resection	216 00	ffff	Arterial popliteal embolectomy, with sympathetic block	135 00
ww	Lahey's resection (two stages)	270 00	gggg	Arterial iliac embolectomy, with sympathetic block	216 00
xx	Colostomy, with posterior resection (two stages)	270 00	hhhh	Malignant melanoma	
yy	Ulcerative colitis			(1) Removal	108 00
	(1) Ileostomy	108 00		(2) Removal, with axillary dissection	162 00
	(2) Resections of large intestine (each stage)	108 00		(3) Removal, with neck dissection	162 00
zz	Diverticulitis			(4) Removal, with groin dissection	216 00
	(1) Drainage of abscess	135 00	uuu	Soft-tissue sarcoma, superficial	
	(2) Drainage and colostomy	189 00		(1) Removal	108 00
aaa	Closure of vesicocolic fistula (all stages)	270 00		(2) Removal, with axillary dissection	162 00
bbb	Closure of colostomy other than above	108 00		(3) Removal, with neck dissection	162 00
ccc	Closure of cecostomy	108 00		(4) Removal, with groin dissection	216 00
ddd	Jejunostomy	108 00	5	Surgery of Hand and Forearm	
eee	Closure of fistula small intestine	135 00	a	Dressings — particularly first one done after extensive operation in which complicated pieces of apparatus are used for splinting purposes, if requiring an hour	27 00
fff	Repair of hernia		b	First aid	
	(1) Ventral	108 00		(1) Management of so-called simple wounds not requiring sutures	5 40
	(2) Inguinal	108 00		(2) Treatment of wounds requiring suturing of skin excluding tendons and nerves — in physician's office or treatment room	27 00
	(3) Femoral	108 00	c	Incision and drainage	
	(4) Sliding inguinal	135 00		(1) Furuncle	10 80
	(5) Bilateral inguinal	162 00		(2) Carbuncle	27 00
	(6) Bilateral femoral	162 00		(3) Paronychia	10 80
	(7) Recurrent	162 00		(4) Subungual abscess	10 80
	(8) Recurrent, with fascial repair	189 00		(5) Pulp-space infection	27 00
	(9) Strangulated	162 00		(6) Osteomyelitis (terminal phalanx)	54 00
	(10) Strangulated, with resection of small intestine	216 00		(7) Sepic finger, joint	27 00
	(11) Incarcerated umbilical hernia	162 00		(8) Tendon-sheath infection (1st, 2nd or 3rd fingers)	54 00
	(12) Diaphragmatic, transpleural or transperitoneal	216 00		(9) Tendon-sheath infection (thumb or ring finger)	108 00
ggg	Pentoneoscopy	54 00		(10) Thenar-space abscess	54 00
	(1) With biopsy	81 00		(11) Midpalmar-space abscess	54 00
hhh	Paracentesis, abdominal	10 00		(12) Cellulitis (dorsum of hand)	27 00
iii	Excision of ulcer, with grafting	108 00		(13) Cellulitis (forearm)	54 00
jjj	Kondoleon's operation (each operation)	108 00		(14) Infected bursa (elbow)	54 00
kkk	Breast		d	Debridement, extensive, with suturing with or without manipulation of fractures and application of specially prepared splints	162 00
	(1) Biopsy, male or female	37 80	e	Plastic, traumatic amputation	
	(2) Simple mastectomy			(1) One finger	81 00
	(a) Male	54 00		(2) Two or more fingers	135 00
	(b) Female	81 00	f	Fractures of finger	
	(3) Abscess, drainage	37 80		(1) Simple	10 80
	(4) Radical mastectomy	162 00		(2) Requiring manipulation	21 60
	(5) Adenoma, removal	54 00		(3) Each additional finger	17 20
	(6) Implantation of radium	54 00		(4) Compound	
lll	Lipectomy	37 80		(a) One finger	54 00
mmm	Sebaceous cyst	21 60		(b) Two or more fingers	108 00
nnn	Incision and drainage of infected cyst	16 20		(c) Involving joint	108 00
ooo	Blood transfusion	27 00	6	Infantile Paralysis (Orthopedic Care)	
ppp	Biopsy		a	Hospital care (operative fees shall include all preoperative and postoperative hospital care, but not subsequent office visits)	
	(1) Muscle	27 00		(1) Nonoperative care of patient (per day)	5 40
	(2) Bone	81 00		(2) Operative cases remaining in hospital after 3 weeks (per day)	2 16
	(3) Sternum	27 00		(3) Total compensation for all hospital care not in any case to exceed (unless special arrangements are made)	
qqq	Incision and drainage of pilonidal abscess	27 00			216 00
rrr	Excision pilonidal cyst or sinus	81 00	b	Equinus	54 00
sss	Dupuytren's contraction	135 00	c	Tenotomy	54 00
ttt	Repair of tendon		d	Foot stabilization	162 00
	(1) One	108 00	e	Tendon transplantation	162 00
	(2) Two	162 00			
	(3) Three	216 00			
	(4) Four or more	270 00			
nnn	Excision of ingrowing toe nail				
	(1) Single	27 00			
	(2) Bilateral	54 00			
vvv	Lumbar puncture	10 80			
www	Chest tap	27 00			
xxx	Amputation				
	(1) Gangrenous lower leg	108 00			
	(2) Thigh	135 00			
	(3) Toe	57 80			

(1) Shoulder for trapezius	162 00	(4) In spinal cord or cauda equina tumors or both	
(2) Elbow for triceps and biceps	108 00	(a) For exposure of tumor	324 00
(3) Forearm and hand		(5) In the treatment of pain and malignant disease	
(a) One muscle	108 00	(a) For nerve section	270 00
(b) Each additional muscle	21 60	(b) For cordotomy	270 00
(4) Lower extremity		c Operations on the sympathetic nervous system	
(a) Erector spinal transplant	216 00	(1) Unilateral resection	216 00
(b) Gluteus medius	162 00	(2) Bilateral resection	324 00
(c) Quadriceps	162 00	(3) Presacral-plexus resection	216 00
(d) Peroneal or posterior tibial	81 00	d Peripheral-nerve operations	
(e) Extensor hallucis	54 00	(1) Suture, decompression and transplantation (one or more) of single and multiple nerves	324 00
7 Neurosurgery		(2) Surgical therapy of painful amputation stumps	270 00
a Craniology		c Diagnostic procedures	
(1) In cranial or intracranial injuries or both		(1) Queckenstedt test	10 80
(a) For depressed fractures	270 00	(2) Cystometrogram	54 00
(b) For compound fractures	270 00	(3) Myelogram (plus x-ray fee)	54 00
(1) With C S F rhinorrhea	270 00	(4) Ventriculogram or ventriculostomy (plus x-ray fee)	54 00
(2) Into frontal sinus	270 00	(5) Pneumoencephalogram (plus x-ray fee)	37 80
(c) For extradural hematomas	270 00	(6) Visualization of intracranial aneurysm by intracarotid injection of dye (plus x-ray fee)	108 00
(d) For subdural hematomas	270 00	f Other procedures and conditions	
(e) For intracortical clots	270 00	(1) Débridement and secondary closure of bed or pressure sores	216 00
(f) For exploratory trephination		(2) Débridement and suture of scalp wounds	54 00
(1) One side	108 00	(3) Therapy of simple nonoperable brain injury with or without associated cranial fracture	108 00
(2) Two sides	162 00	(4) Therapy of simple nonoperable injury of spinal cord or cauda equina or both	378 00
(2) In cranial or intracranial infection or both		(5) Carotid ligation for intracranial arteriovenous fistula or an aneurysm	108 00
(a) For osteomyelitis of skull	216 00	(6) Operation for scalenus anticus syndrome	216 00
(b) For brain abscess	216 00	(7) Intraspinal, paravertebral or paracranial alcohol injection	37 80
(3) In cranial or intracranial congenital defects or both		8 Obstetrics and gynecology	
(a) For oxycephaly	324 00	a Consultations	
(b) For platybasia	324 00	(1) Office, with examination and consultation	10 80
(c) For hydrocephalus		(2) Subsequent office examination	5 40
(1) Choroidectomy	162 00	(3) Cauterization of cervix	16 20
(2) Torkelson operation	270 00	(4) Insufflation of fallopian tubes	16 20
(3) Third ventriculostomy	324 00	(5) Biopsy (cervix or endometrium)	16 20
(d) For excision of encephalocele	324 00	(6) Hospital	108 00
(4) In cranial or intracranial tumors or both		b Delivery — pelvic	
(a) For surgical therapy of tumor	378 00	c Operations	
(b) For intracranial exposure of aneurysm	378 00	(1) Dilatation and curettage of uterus	54 00
(5) In the treatment of pain and malignant disease		(2) Cesarean section (any type)	162 00
(a) For section of the sensory root of the		(3) Ectopic pregnancy	145 00
(1) Fifth cranial nerve	216 00	(4) Hysterectomy (supracervical)	162 00
(2) Transmastoid route	216 00	(5) Complete hysterectomy	162 00
(3) Through the posterior fossa	270 00	(6) Vaginal hysterectomy	162 00
(4) Intramedullary	324 00	(7) Complete hysterectomy (Wertheim operation)	270 00
(b) For section of the vestibular nerve	270 00	(8) Myomectomy	135 00
(c) For combined section of the fifth and ninth cranial nerves	270 00	(9) Uterine suspension	108 00
(d) For medullectomy	324 00	(a) Simple	
(6) In miscellaneous cranial or intracranial conditions or both		(b) With dilatation and curettage or vaginal plastic	135 00
(a) For repair of skull defect	324 00	(c) With appendectomy or adnexal surgery	135 00
(b) For excision of cortical scar	324 00	(d) With plastic surgery and adnexal surgery	135 00
(c) For ablation of cortex	324 00	(10) Removal of ovarian cyst	135 00
(d) For frontal lobotomy	270 00	(11) Presacral neurectomy dilatation and curettage, with or without suspension	162 00
(e) For bilateral orbital decompression	324 00	(12) Salpingectomy, with or without oophorectomy	135 00
b Laminectomy		(13) Bartholin's gland	
(1) In spinal cord or cauda equina injuries or both		(a) Incision	10 80
(a) For compounded wound	324 00	(b) Excision	54 00
(b) For decompression	216 00	(14) Urethral caruncle	27 00
(c) For removal of, or exploration for, an extruded nucleus pulposus or ruptured intervertebral disk	324 00	(15) Removal of labial cysts and tumors	37 80
(d) For anterior rhizotomy in the treatment of transverse myelitis	324 00	(16) Correction of atresia of vagina	162 00
(2) In spinal cord or cauda equina infections or both		(17) Hymenectomy	27 00
(a) For drainage of abscess	216 00	(18) Posterior colpoperineorrhaphy	81 00
(b) For anterior rhizotomy in the treatment of transverse myelitis	324 00		
(3) In spinal cord or cauda equina congenital defects or both			
(a) For excision and repair of meningocele or meningomyelocele or both	162 00		

(19) Amputation of cervix or trachelorrhaphy	81 00	d Osteomyelitis	
(20) Anterior colporrhaphy	81 00	(1) Chronic, 8 weeks' period of treatment	245 00
(21) Anterior colporrhaphy—perineorrhaphy	108 00	(2) Acute, 20 weeks' period of treatment	324 00
(22) Manchester operation	135 00	e Cellulitis, incision and drainage, 2 weeks' period of treatment	
(23) Watkins's operation	162 00	(1) Intraoral	70 20
(24) Colpocleisis (partial or complete)	135 00	(2) Extraoral	108 00
(25) Plastic for functional incontinence of urine	135 00	f Cysts	
(26) Rectovaginal fistula	135 00	(1) Soft tissue	81 00
(27) Vesicovaginal fistula	162 00	(2) Bone	162 00
(28) Cul-de-sac drainage	37 80	g Removal of teeth	
(29) Cauterization or conization of cervix	27 00	(1) Simple	16 20
(30) Uterine polypectomy	27 00	(2) Surgical	37 80
(31) Vulvectomy		(3) Impacted	81 00
(a) Simple	108 00	(4) Complete month	135 00
(b) Radical	162 00	h Apicoectomy	54 00
(32) Correction of uterine displacement and insertion of pessary	10 80	i Alveolotomy	108 00
9 Ophthalmology		j Frenum, lip or tongue	54 00
a Consultations		k Dislocation of mandible, immobilization for	135 00
(1) Office		l Alveolar antral opening, plastic repair of	108 00
(a) Initial visit	10 80	m Alveolar abscess, incision and drainage of	37 80
(b) Subsequent visits	5 40	n Foreign body in jaw	108 00
(2) Outside office		o Biopsy	
(a) Within 10 miles	27 00	(1) Soft tissue	37 80
(b) Beyond 10 miles (add per mile)	1 08	(2) Bone	54 00
b Operations		p Surgical reattachment of muscle	70 20
(1) Removal of foreign body embedded in cornea	5 40	q Vincent's angina, 2 weeks' period of treatment	81 00
(2) Removal of intraocular foreign body	135 00	r Tic douloureux	
(3) Repair of conjunctival laceration	27 00	(1) Alcohol injection	54 00
(4) Suturing of perforating wound of globe and iridectomy, if needed	108 00	(2) Resection of nerve trunk	189 00
(5) Peritomy	27 00	s Oral antral infection, 3 weeks' period of treatment	162 00
(6) Optical iridectomy	108 00	t Gingivectomy, quarter area (surgery or electro-coagulation)	135 00
(7) Chalazion, incision and curettage	16 20	u Periodontosis, 2 weeks' period of treatment	108 00
(8) Corneal ulcer		v Sialolithotomy	81 00
(a) Conjunctival flap for	54 00	w Osteotomy	108 00
(b) Keratotomy for	27 00	x Tumors	
(c) Cauterization or pasteurization of	27 00	(1) Benign	81 00
(9) Keratectomy (for corneal scar)	81 00	(2) Malignant	216 00
(10) Corneal transplantation	216 00	y Osteoarthrotomy	189 00
(11) Cataract		z. Plastic surgery reconstruction of ridge	162 00
(a) Needling — as often as necessary	108 00	(1) With Thiersch-graft implant	216 00
(b) Removal, including needed dissections	162 00	aa Granuloma, curettage of	37 80
(c) Dissection of secondary cataract	54 00	bb Bone graft	216 00
(12) Iridotomy for blocked pupil	81 00	11 Orthopedic surgery	
(13) Lachrymal sac, excision of	81 00	a Biopsy, bone, operative	54 00
(14) Probing of lachrymal duct (in office)	10 80	b Casts (plaster or similar material), not including first application with reduction or operation	
(15) Probing of congenital obstruction of lachrymal duct	27 00	(1) Forearm	16 20
(16) Dacryocystorhinostomy	162 00	(2) Entire arm	21 60
(17) Incision for acute dacryocystitis	16 20	(3) Shoulder spica	43 00
(18) Glaucoma		(4) Leg to knee	16 20
(a) Acute — iridectomy	162 00	(5) Leg to groin	21 60
(b) Chronic		(6) Leg spica	54 00
(1) Filtration operation	162 00	(7) Plaster jacket	54 00
(2) Cyclodiathermy	81 00	(a) Including head	64 80
(19) Paracentesis	54 00	c Fractures	
(20) Tarsorrhaphy	54 00	(1) Simple	
(21) Ptoxis, operation	162 00	(a) Nose	16 20
(22) Ectropion, operation	108 00	(b) Maxilla, inferior	27 00
(23) Entropion, operation	54 00	(c) Maxilla, superior	16 20
(24) Snellen suture for entropion or ectropion	16 20	(d) Spine	162 00
(25) Scalping lid margin for trichiasis	54 00	(e) Ribs	10 80
(26) Retinal separation (as many as needed)	162 00	(f) Clavicle	54 00
(27) Enucleation or evisceration of globe	108 00	(g) Scapula	54 00
(28) Exenteration of orbit	216 00	(h) Humerus	108 00
10 Oral and maxillofacial surgery		(i) Elbow (excepting head of radius)	81 00
a. Diagnostic workup		(j) Radius and ulna shaft	108 00
(1) Hospital	54 00	(k) Radius, shaft only	81 00
(2) Office	37 80	(l) Colles's fracture	
b Vitalization test (complete)	37 80	(1) Closed	70 20
c Fractures (mandible, maxilla, nasal and malar bones), 6 weeks' period of treatment		(2) Open	118 00
(1) Simple	189 00	(m) Ulna, shaft only	54 00
(2) Compound	243 00	(n) Radius, head of	54 00
(3) Multiple	324 00		

(o) Metacarpals			(17) Subastragalus	54 00
(1) Single bone or any or all of middle three	27 00		(18) Mediotarsal	54 00
(2) Each extra metacarpal	5 40		(19) Metatarsal bone	
(p) Carpal bone, one	27 00		(a) One	5 40
(q) Scaphoid, closed	32 40		(b) Each additional	5 40
(r) Finger			(20) Toe	
(1) One	21 60		(a) One	5 40
(2) Each extra	16 20		(b) Each additional	5 40
(s) Pelvis	108 00		e Joint resections	
(t) Femur			(1) Shoulder	162 00
(1) Shaft including supracondylar	162 00		(2) Elbow	108 00
(2) Intracapsular	216 00		(3) Wrist	108 00
(3) Intertrochanteric	162 00		(4) Hip	162 00
(u) Tibia, shaft	81 00		(5) Ankle	162 00
(v) Tibia, involving knee joint	162 00		(6) Complete rupture of supraspinatus tendon	189 00
(w) Shaft of fibula	27 00		f Orthopedic operations	
(x) Tibia and fibula (including Pott's fracture)	108 00		(1) Spinal fusion	216 00
(1) Trimalleolar	162 00		(2) Talipes	162 00
(y) Fracture of patella (simple)	54 00		(3) Tenotomy	54 00
(z) Metatarsal bone			(4) Tenorrhaphy	108 00
(1) One	32 40		(5) Arthrotomy, any major joint	108 00
(2) Each additional	10 80		(6) Acute osteomyelitis	162 00
(aa) Tarsal bone, one, excluding os calcis and astragalus	27 00		(7) Chronic osteomyelitis, sequestrum removal	162 00
(bb) Os calcis and subastragalus, each	162 00		(8) Foot stabilization	162 00
(cc) Great toe	10 80		(9) Arthrodesis of knee, shoulder or elbow	162 00
(2) In fractures requiring an open reduction, the maximum amount of reimbursement will be twice the amount shown for simple fractures except for Colles fracture (see above), up to	162 00		(10) Arthroplasty, any major joint	162 00
(3) The fees for all compound fractures are double those of simple fractures			(11) Arthrodesis of hip	216 00
d Dislocations, fresh			g Amputations	
(1) Spine	189 00		(1) Shoulder	108 00
(2) Maxilla, inferior	27 00		(2) Hand	108 00
(3) Clavicle			(3) Hip	162 00
(a) Simple	54 00		(4) Knee	162 00
(b) Requiring open operation	108 00		(5) Leg	162 00
(4) Shoulder	54 00		(6) Foot	108 00
(5) Elbow	54 00		(7) Elbow	108 00
(6) Shoulder and elbow, requiring open operation	162 00		(8) Arm	
(7) Wrist	81 00		(a) Disarticulation, uncomplicated	162 00
(8) Metacarpal bone			(b) Head or neck	108 00
(a) One	16 20		(c) Below neck	81 00
(b) Each extra	5 40		(9) Hand at wrist	108 00
(c) Requiring open operation, charges are doubled			(10) Carpus	64 00
(9) First metacarpophalangeal joint			(11) Metacarpus	54 00
(a) Simple	21 60		(12) Phalanx	32 40
(b) Requiring open operation	81 00		(13) Thigh, disarticulation	162 00
(10) Carpal bone			(14) Leg at knee	108 00
(a) One	27 00		(15) Patella, excision	81 00
(b) One or more, open operation	81 00		(16) Femur, head and neck	162 00
(11) Finger			(17) Tibia or fibula	108 00
(a) Simple			(18) Foot, metatarsus	81 00
(1) One	5 40		(19) Os calcis (Syme's amputation)	108 00
(2) Each additional	5 40		(20) Phalanx (toe)	32 40
(b) Requiring open operation	5 40		(21) Astragalectomy	108 00
(1) One	10 80		(22) Laminectomy or other osteoplastic	216 00
(2) Each additional	10 80		(23) Coccyx, removal	81 00
(12) Hip			(24) Spinal fusion, involving bone inlay	216 00
(a) Simple	108 00		(25) Removal of semilunar cartilage	108 00
(b) Requiring open operation	162 00		(26) Rib excision or resection	54 00
(13) Knee			(27) Arthrodesis, wrist	162 00
(a) Simple	108 00		(28) Bone graft — including postoperative therapy	
(b) Requiring open operation	162 00		(a) For non-union of femur	270 00
(14) Knee, semilunar cartilage			(b) For non-union of tibia	216 00
(a) Simple	27 00		(c) Humerus	189 00
(b) Requiring open operation	162 00		(d) Forearm	189 00
(15) Tarsal bones, excepting astragalus and os calcis			h Ganglion, excision of	
(a) Simple	27 00		(1) Simple	27 00
(b) Requiring open operation	54 00		(2) Involving joint	54 00
(16) Tibioastragalus	54 00		12 Otolaryngology	
			a Endoscopy	
			(1) Bronchoscopy	
			(a) Diagnostic	27 00
			(b) Therapeutic	27 00
			(1) Bronchoscopic aspiration	27 00
			(2) Removal of tumor or implantation of radium	135 00
			(3) Removal of foreign body	135 00
			(2) Esophagoscopy, observation	27 00
			(3) Bronchogram	27 00

13 Burns

- b Second degree (if first-degree burn is also present there is no extra charge) Pay is according to the following schedules, whichever is lower

Code	Description	Charge	Area sq in	Day or Care	Charge	Cumulative Charge
(a)	Base of tongue	70 20				
(b)	Epiglottis	70 20				
(c)	Floor of mouth	70 20				
(d)	Larynx	189 00				
(e)	Ludwig's angina	162 00				
(f)	Orbital (external ethmoidectomy)	216 00				
(g)	Pharyngomaxillary fossa	162 00				
(h)	Peritonsillar	70 20				
(i)	Retropharyngeal	70 20				
(2)	Adenoidectomy	54 00				
(3)	Ethmoid operations					
(a)	External exenteration	162 00				
(b)	Intranasal exenteration	108 00				
(4)	Frontal osteomyelitis, removal of frontal bone	270 00				
(5)	Frontal sinus operations					
(a)	Intranasal operation	108 00				
(b)	Killian operation	270 00				
(c)	Lynch operation	270 00				
(d)	Obliteration operation	270 00				
(e)	Sewall operation	270 00				
(f)	Skullern operation	270 00				
(6)	Larynx operations					
(a)	Direct laryngoscopy	70 20				
(b)	Direct laryngoscopy and biopsy	108 00				
(c)	Laryngectomy	270 00				
(d)	Laryngofissure	270 00				
(e)	Lynch suspension	135 00				
(f)	Removal of benign growth	135 00				
(g)	Removal of foreign body	135 00				
(7)	Malignant disease of sinuses					
(a)	Lateral rhinotomy	270 00				
(b)	Exenteration of orbit	270 00				
(c)	Moure operation	270 00				
(8)	Maxillary-antrum operations					
(a)	Antrotomy (intranasal)	81 00				
(b)	Caldwell-Luc operation	162 00				
(c)	Denker operation	162 00				
(9)	Nasal polyps, removal	54 00				
(10)	Nasal-septum operations					
(a)	Cauterization	37 80				
(b)	Setting of fracture	54 00				
(c)	Submucous resection	135 00				
(11)	Salivary-gland operations					
(a)	Incision and drainage	81 00				
(b)	Removal of calculus from duct	81 00				
(12)	Tear-sac (Toti-Mosher) operation	216 00				
(13)	Tonsillectomy	81 00				
(14)	Tonsillectomy and adenoidectomy	81 00				
(15)	Tracheotomy	108 00				
(16)	Turbinate, submucous cauterization	16 20				
c.	Ear operations					
(1)	Brain abscess	270 00				
(2)	Jugular ligations	270 00				
(3)	Lateral sinus, drainage of	270 00				
(4)	Mastoidectomy					
(a)	Simple	216 00				
(b)	Radical	270 00				
(5)	Fenestration	270 00				
(6)	Ossiculectomy	162 00				
(7)	Paracentesis	27 00				
(8)	Polypectomy	54 00				
(9)	Postaural abscess, incision and drainage	54 00				
(10)	Petrositis, drainage	270 00				
(11)	Foreign body					
(a)	In ear canal	27 00				
(b)	In nose	27 00				
(c)	In pharynx	37 80				
d.	Minor treatments					
(1)	Electrocoagulation of turbinates	16 20				
(2)	Antrum wash	27 00				
(3)	Electrocoagulation of pharyngeal lymphoid tissue	27 00				
(4)	Biopsy from nose	37 80				
e.	Consultations (see Internal Medicine)					

f	Repair following facial paralysis	216 00	(13)	Tumors, trauma or infection of thoracic cage, with resection of one rib or multiple ribs and plastic closure	270 00
(1)	Subsequent operation	108 00	(14)	Pectus excavatum (operative correction)	270 00
g	Arthroplasty (for ankylosis of jaw)	270 00	(15)	Chest trauma, rib fractures	
h	Operation for prognathism of jaw	270 00	(a)	Nonoperative treatment	27 00
i	Operation for retrusion of jaw	270 00	(b)	Operative treatment	216 00
j	Construction of special splints for the last two mentioned operations	108 00	(16)	Penetrating wounds of chest (open thoracotomy)	324 00
k	Avulsion of scalp (plastic repair) (each operation)	216 00	(17)	Thoracotomy for intrathoracic vascular injuries of aneurysm	324 00
l	Atresia of nasopharynx (each operation)	216 00	b	Heart and pericardium	
m	Congenital closure of posterior choanae (each operation)	216 00	(1)	Pericardium, paracentesis	54 00
15	Proctology		(2)	Pericardiostomy	270 00
a	Office procedures		(3)	Pericardiectomy	378 00
(1)	Proctoscopy, with biopsy and pathological examination	16 20	(4)	Cardiomyopexy	378 00
(2)	Injection of hemorrhoids	21 60	(5)	Cardio-omentopexy	378 00
b	Operations		(6)	Cardiopercardialpexy (pericardial poudrage)	216 00
(1)	Office		(7)	Cardiac suture, post-traumatic	378 00
(a)	Incision and drainage of abscess	16 20	(8)	Foreign body, heart or pericardium, removal of	378 00
(b)	Excision of single thrombosed hemorrhoid	16 20	(9)	Division of patent ductus arteriosus	324 00
(c)	Excision of external tag	16 20	(10)	Thoracotomy for excision coarctation of aorta	378 00
(d)	Oil injection, fissure	10 80	c	Diaphragm	
(e)	Removal of papilla	16 20	(1)	Traumatic rupture, repair	270 00
(2)	Hospital		(2)	Diaphragmatic hernia, repair	270 00
(a)	Hemorrhoidectomy		(3)	Hiatus hernia, repair	270 00
(1)	External	27 00	(4)	Abscess, subphrenic, drainage	162 00
(2)	External and internal	81 00	(5)	Abscess of liver, drainage	162 00
(b)	Sphincter dilatation	27 00	d	Esophagus and stomach	
(c)	Excision of mucous membrane (prolapse)	81 00	(1)	Transthoracic gastric resection	378 00
(d)	Excision of fissure-in-ano	54 00	(2)	Transthoracic resection	378 00
(e)	Incision, simple fistulectomy	108 00	(3)	Transthoracic vagotomy and associated procedures	378 00
(f)	Excision of fissure-in-ano, with dilatation and cryptectomy	81 00	17	Physiotherapy	
(g)	Incision, recurrent of complicated fistula	135 00	a	Consultations, office	10 80
(h)	Incision of anal stricture	54 00	(1)	Initial	
(i)	Incision and drainage of perineal abscess	37 80	(2)	Subsequent visits — covering such of the following as indicated long-wave diathermy (approximately 20 minutes), short-wave diathermy (approximately 12 to 16 minutes), ultraviolet ray, water cooled (approximately 10 seconds to 2 minutes) and air cooled (approximately 15 seconds to 13 minutes), negative and positive galvanism (approximately 3 minutes to 20 seconds), slow sinusoidal therapy (approximately 3 minutes to 10 minutes), whirlpool bath (approximately 10 minutes to 15 minutes), radiant heat, 1000-watt lamp or infrared lamp (approximately 20 minutes), cabinet bath (approximately 20 minutes), and test for reaction of degeneration faradic condenser discharge and massage and motion (no time element involved, this depending on co-operation of patient, parts involved, diagnosis, etc.)	5 40
(j)	Repair of anal sphincter	108 00	18	Urologic surgery	
(k)	Complete prolapse of rectum, cauterization	81 00	a	Cystoscopy	
(l)	Alcohol injection for pruritus	54 00	(1)	Observation	21 60
16	Thoracic surgery		(2)	With ureteral catheter	27 00
a	Lungs, pleura and mediastinum		(3)	With ureteral catheter and retrograde pyelogram	37 80
(1)	Pleura, paracentesis, for diagnosis	27 00	(4)	Operative, with fulguration, etc	54 00
(2)	Artificial intrapleural pneumothorax		b	Urethrotomy	
(a)	Initial fill	27 00	(1)	Internal	54 00
(b)	All subsequent refills	10 80	(2)	External	81 00
(3)	Extrapleural pneumonolysis with associated procedures	270 00	c	Prostatectomy	
(a)	Subsequent refills (extrapleural pneumothorax)	10 80	(1)	Perineal	189 00
(4)	Intrapleural pneumonolysis		(2)	Transurethral	162 00
(a)	Open thoracotomy	216 00	(3)	One-stage suprapubic	162 00
(b)	Under thoracoscopic control, diagnostic or therapeutic	135 00	(4)	Two-stage suprapubic	216 00
(5)	Phrenic-nerve paralysis (independent operation)	108 00	d	Prostatic abscess	54 00
(6)	Empyema		e	Hydrocele	81 00
(a)	Closed drainage	108 00	f	Epididymotomy	54 00
(b)	Thoracostomy	162 00	g	Epididymectomy	81 00
(7)	Decortication of lung	270 00			
(8)	Thoracoplasty				
(a)	One-stage operation	162 00			
(b)	Two or more stages	324 00			
(c)	Schede operation for chronic empyema	270 00			
(9)	Pneumectomy, with associated procedures for any disease	378 00			
(10)	Lobectomy, with associated procedures for any disease	378 00			
(11)	Cavernostomy of lung for abscess (one or two stages)	324 00			
(12)	Thoracotomy				
(a)	For mediastinal tumors or cysts (removal)	378 00			
(b)	Exploratory, for inoperable intrathoracic tumors	270 00			
(c)	For intrathoracic injuries	324 00			

h Vesiculectomy	189 00	dd Hypospadias or epispadias repair	
i Repair of varicocele	54 00	(1) One stage	216 00
j Orchidopexy	108 00	(2) Two or more stages (each stage)	135 00
k. Orchidectomy		ee. Meatotomy	21 00
(1) Single	54 00	ff Caruncle excision	54 00
(2) With lymph-node dissection	108 00	(1) With fulguration	27 00
(3) Bilateral	81 00	gg Perineal implantation of radium, prostate	108 00
l Cystotomy	108 00	hh Urethral dilatation	10 80
(1) With radium, fulguration or removal of calculus	135 00	ii Circumcision	21 60
m Cystectomy	162 00	19 Vascular surgery	
n Cystectomy and ureterointestinal anastomosis (one stage)	270 00	a Varicose veins	
o Ureterostomy	135 00	(1) Unilateral ligation, saphenous	
p Ureterolithotomy	162 00	(a) High, low and multiple	81 00
q Perirenal abscess, incision and drainage	108 00	(b) High, with dissection of perforating veins	108 00
r Nephrostomy	162 00	(c) High, with dissection of perforating veins and skin graft	135 00
s Nephrotomy	162 00	(2) Bilateral ligation, saphenous	
t Nephropexy	162 00	(a) High, low and multiple	135 00
n Nephrectomy		(b) High, with dissection of perforating veins	189 00
(1) Simple	162 00	(c) High, with dissection of perforating veins with skin graft	216 00
(2) For tumor	189 00	(3) Office treatment of varicose veins and complications (per visit)	5 40
v Nephroureterectomy	189 00	b Femoral veins	
w Pyelotomy	162 00	(1) Unilateral division	108 00
x Plastic operation on ureter or renal pelvis	189 00	(2) Bilateral division	162 00
y Removal of solitary cyst	162 00	c. Iliac veins	
z. Heminephrectomy	189 00	(1) Unilateral division	108 00
aa Vesicovaginal fistula	162 00	(2) Bilateral division	162 00
bb Perineal fistula	135 00	d Inferior vena cava, division of	216 00
cc Amputation of penis		e Procaine sympathetic block	
(1) Partial	108 00	(1) Lumbar	16 20
(2) Complete	135 00	(2) Thoracic	27 00
(3) With groin dissection	162 00		

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32301

PRESENTATION OF CASE

First admission A sixty-three-year-old steam fitter entered the hospital because of hoarseness.

For years the patient had had a cough productive of small amounts of whitish sputum. A year before entry he began to notice intermittent attacks of hoarseness without accompanying dyspnea or hemoptysis. About the same time he also had a single bout of difficulty in swallowing. The hoarseness progressed for six months, remaining constant thereafter. He had lost about 15 pounds during the preceding two years.

The patient had always been well and strong except for an attack of "pneumonia" thirty years previously.

Physical examination revealed a moderately well nourished man. The larynx showed a thickened right vocal cord covered with whitish hyperkeratotic nodules extending toward the anterior commissure, where a soft polyp was visible. The left cord was slightly injected. The mobility of the larynx on swallowing was not impaired. There were a few, small, nontender cervical nodes. The mid-dorsal spine showed a moderate kyphosis. The chest was emphysematous, with increased anteroposterior diameter. One observer thought that it was slightly smaller on the left than on the right and that it lagged somewhat during respiratory movement. There were a few scattered rales over the left upper lung field. The diaphragm moved well. The heart appeared to be slightly enlarged, with both systolic and diastolic murmurs at the base and apex. The abdomen and extremities were normal.

The temperature, pulse and respirations were normal. The blood pressure was 108 systolic, 94 diastolic.

Examination of the blood showed a red-cell count of 3,980,000, with 12.2 gm. of hemoglobin, and a white-cell count of 5300, with 56 per cent neutrophils, 36 per cent lymphocytes and 6 per cent monocytes. The sedimentation rate was 30 mm. in thirty minutes, and 48 mm. in sixty minutes. Examination of the urine was negative.

An x-ray film of the chest revealed an area of infiltration in the left apex and considerable thickening in the left hilus. A sputum smear was negative for acid-fast organisms. A biopsy of the right vocal cord was reported as showing a Grade II epidermoid carcinoma. The patient was discharged to be readmitted for total laryngectomy.

Second admission (one month later) Another x-ray film of the chest revealed infiltration in both apexes that was interpreted as "probably active." Two sputum smears were negative for acid-fast organisms, but guinea-pig inoculation gave a positive reaction.

The patient was discharged to a sanatorium.

Third admission (three months later) Since the patient's tuberculosis was thought to have been arrested, he was admitted for total laryngectomy. Physical examination and x-ray study of the chest were essentially the same as on the previous admission. The operation was uneventful. The pathological report was Grade II epidermoid carcinoma, with metastases to regional lymph nodes.

The patient did well postoperatively, receiving 24,000 units of penicillin every three hours for thirteen days. On the fifteenth postoperative day, while sitting on the toilet, he was suddenly seized by an extremely severe pain in the epigastrium. He motioned for help, and while being assisted back to the ward, he collapsed on the floor. He was pale, writhing in pain and sweating profusely. When queried about the location of the pain, he repeatedly pointed to the epigastrium, chiefly in the midline. The lips had a grayish hue. He vomited a small amount of coffee-grounds material. Examination of the chest revealed only a few rhonchi at the left base. The heart had not changed since the previous examination. The abdomen was spastic throughout, particularly in the epigastrium. There was also exquisite rebound tenderness throughout, most marked in the left upper quadrant and midepigastrium, and referred from the right lower quadrant to below the xiphoid. Peristalsis was absent. No masses could be made out. There was no arm, shoulder, chest or neck pain. Pain was not increased by respiration, and there was no cough. When asked specifically, the patient denied that there was an element of substernal compression, tightness in the chest or difficult breathing. It was deduced by devious questioning — to which he could only indicate assent or negation — that the pain was constant, unremitting, nonradiating and of great severity, that it was unassociated with a desire to urinate or defecate and that its location was strictly in the upper abdomen.

Examination of the blood showed a white-cell count of 16,100. A stool specimen obtained during rectal examination was guaiac positive.

An x-ray film of the chest showed mottled areas of increased density in both lower lung fields, in addition to calcified areas at the apexes. The vascular

shadows were prominent in both hilar regions, and there appeared to be some haziness in the right upper mediastinum. The abdomen showed no evidence of dilated loops. There was a small amount of gas and much fecal material in the large bowel.

An electrocardiogram showed evidence of chronic coronary disease but none of an acute process.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. OLIVER COPE Of course, from the record, only one thing can explain the situation. The patient had an operation and survived. The one lesion that fits with that history is a perforated peptic ulcer. That diagnosis may be too easy, and therefore I had better see the x-ray films.

DR. JAMES R. LINGLEY These first two films, taken at the Eye and Ear Infirmary one month apart, show emphysema and a process at the apex on both sides, more extensive on the left than on the right. It is a hazy type of infiltration. This film, taken just before the abdominal operation and fifteen days following laryngectomy, shows a high diaphragm on both sides and density at both bases, which could be explained by atelectasis from a high diaphragm, and the same process in the apexes. The film of the abdomen shows extensive calcification of the abdominal aorta and the internal iliac arteries. There is an area of calcification over the upper pole of the left kidney, which is interesting in view of the findings in the chest. Unfortunately, we do not have a lateral view, so that I cannot be sure that it is a calcified adrenal gland, in the anteroposterior view the calcification is in the proper position for it, but the explanation may be an overlying calcified lymph node.

DR. COPE They should have written that into the record to make it harder. Is there any evidence of air under the diaphragm?

DR. LINGLEY Since the films were taken in a prone position, I cannot rule out air under the diaphragm.

DR. COPE I say that this was a perforated lesion of the upper gastrointestinal tract because that complication occurs not too infrequently following a major surgical procedure — often enough to be something of which everyone should be aware. The pain, of course, was not typical of anything other than severe irritation, and it may turn out that the patient had a ruptured aortic aneurysm. I assume that he made some effort at the toilet, which was the final push that ruptured something. Effort to defecate could result finally in perforation somewhere in the intestinal tract. Such effort could rupture an abscess or could be the initiating cause of rupture of an aneurysm or of rupture through a weak place somewhere along the aorta. The upper abdominal pain is the typical place for pain to radiate in rupture of the thoracic aorta. Usually, at least in the few patients I have had an opportunity to see in the

differential diagnosis of a surgical lesion, the pain starts not so abruptly, developing quite quickly to a high pitch, however. I shall exclude dissecting aneurysm of the aorta as a diagnosis, because in all probability the patient would not have survived it.

Abdominal tenderness and pain in the epigastrium can of course be produced by a lesion in the chest in the region of the sixth to ninth costal nerves. One can be misled by a lesion in the chest, the abdomen has often been opened for disease above the diaphragm. On the other hand, peristalsis was absent, and there was coffee-grounds material in the stomach, with a positive guaiac test in the stools, which suggest that the lesion was within the gastrointestinal tract. Also, the x-ray studies are not compatible with an abscess of the lung. I have never seen a tuberculous abscess rupture down through the diaphragm. There is only one infectious disease that does go down through the diaphragm — actinomycosis. Subdiaphragmatic abscesses frequently rupture upward through the diaphragm into the chest, but the reverse is rare, except in actinomycotic lesions, actinomycosis being no respecter of anatomic barriers. Tuberculosis, on the other hand, is a respecter of anatomic partitions and does not go downward ordinarily, I shall exclude tuberculosis of the lungs as the cause of this acute painful episode, on the basis of this last chest film, which I interpret as negative so far as the lungs are concerned, and also on the findings related to the abdominal organs.

What about the primary diagnosis that I mentioned — a perforated peptic ulcer? From the history the man had had no ulcer symptoms or indigestion, but the latter might have been missed because of the fact that after laryngectomy there is a problem in feeding and that with any symptoms referable to an acute ulcerative process in the stomach and duodenum, the upper small intestine might easily be missed. Various symptoms have been overlooked in such complicated feeding problems. Acute ulcer of the upper gastrointestinal tract, so-called "peptic ulcer," is not an infrequent lesion following trauma of various sorts. The classic description is Curling's ulcer, the type that follows burn trauma. It also follows other kinds of trauma and acute adrenal insufficiency. Because of the latter I wonder why the finding of the X-ray Department was not recorded, the presence of calcification in an adrenal gland suggests old tuberculous damage. The patient might well have had some degree of adrenocortical insufficiency or failure to respond to operative treatment in a way that would result in what one might call subclinical shock, which could have been the initiating factor of the ulcer. This type of ulceration has received a great deal of attention recently regarding the so-called "alarm reaction,"* which occurs with hemoconcentration, and this man may have had hemoconcentration following laryn-

*Selye, H. General adaptation syndrome and diseases of adaptation. *J. Clin. Endocrinol.* 6:117-230, 1946.

gectomy He had chronic tuberculosis of the lung, which may have prevented a good response to treatment like that of a healthy vigorous person, he had two strikes against him to begin with

I have stuck my neck out a long way I have even gone prematurely into a historical account of acute gastrointestinal ulcer following trauma, but I have done so because I do not see any other alternative I should expect the ulcer that perforated to have been in the stomach or, more probably, in the duodenum It may have been multiple Dr Castleman, you will recall that you and Dr John Bradley had a case several years ago in which on the eighth postoperative day one ulcer perforated at 2:00 a m, a second at 4:30 a m and later a third, which was not recognized clinically but which was found at post-mortem examination Multiple ulcers are a possibility in the case under discussion

DR BENJAMIN CASTLEMAN Are there any comments or other suggestions?

DR WALTER BAUER A perforated peptic ulcer is a likely explanation of the episode of acute pain

DR CASTLEMAN Dr Dahl, will you tell us what your impression was?

DR LEWIS K DAHL From the medical standpoint we went through approximately the same process of reasoning as that of Dr Cope We favored a vascular accident rather than a perforated viscus We thought that the only hope of survival lay in the possibility of a perforated viscus and therefore believed that operation was indicated I think that the surgical men favored a perforated viscus, but it is fair to say that no one considered the actual condition

CLINICAL DIAGNOSIS

Perforated peptic ulcer

DR COPE'S DIAGNOSES

Perforated peptic ulcer

Chronic pulmonary tuberculosis

ANATOMICAL DIAGNOSIS

Negative abdominal exploration

PATHOLOGICAL DISCUSSION

DR CASTLEMAN The abdominal exploration was entirely negative You may have another chance, Dr Cope

DIFFERENTIAL DIAGNOSIS (Continued)

DR COPE The medical side passed it up, and the thing I want to stress again is that the patient survived That is what puzzles me It is not in the record, but I assume that the patient survived the operation as well as the lesion that gave rise to the pain

DR CASTLEMAN The patient did die — about twenty-four hours after operation

DR COPE That makes it somewhat easier because, as I said at the outset, the only curable lesion

that I could think of was a perforated peptic ulcer, which was sutured at operation, but I cannot imagine survival with a dissecting aneurysm of the aorta I suppose that the patient could have survived, but this came on acutely and I suspect that it eventually led to death I do not know enough about that, however

To go back to the tuberculosis, there was undoubtedly active tuberculosis in the chest I can not believe that there was a rupture of an abscess, with formation of empyema There was no displacement of the mediastinum, no cough and no increase in pain on respiration The record also does not suggest that an abscess had ruptured into a bronchus In other words, I do not find evidence of an abscess that broke into a pleural space I can find nothing pointing to the abdomen, and that is substantiated by the fact that the abdominal laparotomy was negative I cannot go any farther with tuberculosis of the lung

A negative electrocardiogram at such a stage, if my understanding is correct, does not exclude a coronary infarction The electrocardiographic changes may not become positive (I hope that I shall be corrected if I am making a wrong statement) for three or four days or possibly longer This could have been coronary occlusion, because absence of the left arm radiation and absence of substernal tightness or compression do not exclude a coronary lesion I must go back to a vascular lesion to explain this episode, and I do not know whether it was a lesion of the aorta — a dissecting aneurysm of the thoracic aorta — or a coronary accident

DR CASTLEMAN The field is still wide open

DR COPE Dr Bauer, you must have an opinion on this

DR BAUER I am stumped

DR COPE I am glad we have that in the record

CLINICAL DIAGNOSIS

Gastrointestinal hemorrhage, cause undetermined
Pancreatitis?

DR. COPE'S DIAGNOSIS

Dissecting aneurysm of aorta?

Coronary thrombosis?

ANATOMICAL DIAGNOSES

Acute fibrinopurulent mediastinitis

Acute fibrinopurulent pleuritis

Chronic pulmonary tuberculosis

Carcinomas of stomach and sigmoid

Chronic tuberculosis of left adrenal gland, with calcification

Operation total laryngectomy for epidermoid carcinoma of larynx

PATHOLOGICAL DISCUSSION

DR CASTLEMAN Before I call on Dr Schall to discuss the operation, let me tell you what was found

at autopsy Surrounding the posterior aspect of the esophagus from about the fourth to the eighth thoracic vertebra, we found an acute mediastinitis, there was about 150 cc of foul-smelling fibrino-purulent material This surrounded the posterior aspect and both sides of the esophagus and extended into both pleural cavities We found 700 cc of purulent fluid in the left chest This abscess of the posterior mediastinum extended downward forming a channel into the right pleural cavity It also extended upward, but not so far up as the tracheotomy There was no connection between the tracheotomy and this infection of the posterior mediastinum We asked Dr Schall about this complication of laryngectomy, and he is here to tell us about it

DR. LEROY A SCHALL The fatal complications of total laryngectomy are hemorrhage and sepsis The sulfonamides and the antibiotics have practically eliminated infection as a complication, and this is the first case of serious infection since the introduction of these agents In 106 cases of total laryngectomy, death occurred in only 3 cases, including this one, from infection Our patients are put on 24,000 units of penicillin every three hours With this patient penicillin was given for twelve days Clinically he did exceptionally well His temperature was normal, the wound healed by first intention, and he was about ready to be discharged

I believe that it is important in doing a laryngectomy to avoid, so far as possible, opening the fascial planes to the mediastinum The posterior attachment of the trachea to the esophagus is not disturbed For this reason I do not do the so-called "pull-through" operation, whereby the trachea is freed and pulled through a buttonhole incision

You may well understand that many patients with cancer of the larynx are poor surgical risks This patient's tuberculosis delayed the operation

The lesson in this case was that of infection masked by penicillin

DR. CASTLEMAN There was no evidence of tuberculosis in the mediastinum, although tuberculosis in the lungs was still quite active There was calcification of the left adrenal gland, due to old tuberculosis Following operation a gastric hemorrhage occurred, which proved to be due to carcinoma of the stomach, there was also a carcinoma of the sigmoid

DR. COPE I gambled on the knowledge of Dr Schall's excellent operative record, but I should have considered mediastinitis on the basis of the x-ray film

DR. LINGLEY There is nothing distinctive in that film There was a high diaphragm which is consistent with mediastinitis

DR. BAUER There is not much in the record to suggest sepsis

DR. SCHALL Nor was there any history of sepsis

DR. CASTLEMAN Would you agree on the apparent masking of the infection by the penicillin?

DR. BAUER Yes The penicillin was stopped on the thirteenth day, and the episode occurred on the fifteenth day There was nothing in the history to indicate the presence of infection, and I also thought that the subsequent widening of the mediastinum was due to a high diaphragm That was consistent with Dr Cope's original diagnosis If I had discussed the case I still should have made the same diagnosis as Dr Cope did — perforated peptic ulcer — and obviously should have been wrong

CASE 32302

PRESENTATION OF CASE

A sixty-five-year-old widow entered the hospital because of severe dyspnea

For over a year the patient had had a chronic cough productive of thin sputum, which was never bloody She was also thought to have lost some weight Five weeks before entry she consulted a physician because of these symptoms She was found to be emaciated, weighing 101 pounds X-ray study showed the heart to be enlarged, and an aortic diastolic murmur was heard Some inflammation of the throat and larynx was present, but there was no x-ray evidence of pulmonary disease The blood pressure was within normal limits, and the urine was normal A week before entry the patient noted swelling of the ankles, and three days later she appeared so thin and exhausted that she was put to bed Her physician prescribed aminophyllin tablets She began to cough up heavy yellowish sputum and ran a temperature ranging between 99 and 101.6° She also complained of discomfort along the right costal margin on coughing, but she had no chills and no sharp pain intensified by inspiration About twenty-four hours before entry she became progressively more dyspneic

On physical examination, the patient was somewhat pale, emaciated and markedly dyspneic, with moderately cyanotic lips and audible tracheal rales She spoke in almost unintelligible snatches between breaths and appeared somewhat confused Most of the history had to be obtained from a companion She was in no greater discomfort when lying on her side or with her back at 30° than when sitting upright The left pupil was somewhat larger than the right, and both pupils appeared slightly irregular The heart was enlarged, the area of dullness extending to the midaxillary line on the left The sounds were strong but partially obscured by loud respiratory noises No murmur or gallop rhythm was made out The radial pulses were weak and thready, with occasional irregularities The chest showed restricted expansion on the right There was dullness to flatness on percussion over the right

lower lung field both anteriorly and posteriorly. Coarse, moist rales were heard throughout the other portions of the chest. The upper abdomen was markedly resistant to palpation, but there was apparently no tenderness and no masses were made out. The extremities were somewhat weak, and there was ++ pitting edema over the lower legs.

The temperature was 100.5°F, the pulse 140, and the respirations 25. The blood pressure was 105 systolic, 70 diastolic.

Examination of the blood showed a white-cell count of 43,200, with 90 per cent neutrophils and a marked shift to the left. No toxic granules were seen. The platelets and red cells appeared normal. Blood cultures were negative. The urine had a specific gravity of 1.020 and showed a + test for albumin, the sediment contained many bacteria and 10 white cells per high-power field.

The patient was given Cedilanid and oxygen, and tourniquets were applied with considerable clearing of the moisture in the left chest and recession of the cardiac apex to the anterior axillary line. Nevertheless she gradually lapsed into shock and stupor. Neo-Synephrine had no appreciable effect on the blood pressure. The respirations became progressively shallower and slower. She died eleven hours after admission.

DIFFERENTIAL DIAGNOSIS

DR. JOHN GRAHAM It seems obvious to me that, whatever else this patient had, she had heart disease. This is attested to by two sets of significant findings, — those of x-ray examination and those of physical examination, — both of which indicated that the heart was enlarged. The other symptoms, such as dyspnea, edema and cough, can conceivably be attributed to other diseases, but that much enlargement of the heart in the absence of severe anemia — and we are told that the red cells appeared normal — indicates serious heart disease. The question in this case is whether there was some lesion in addition to the heart disease.

Several factors suggest that more than cardiac disease was present. The cough with thin sputum might have been consistent with cardiac disease alone. X-ray examination was negative, so far as the lungs were concerned. When she really began to get sick, however, just before coming to the hospital, she began bringing up thick yellow sputum and at the same time began to have a fever as high as 101.6°F and pain in the right chest. On physical examination she had dullness and flatness throughout the right chest, with limited motion and some pain, and dyspnea in all positions. These facts are not particularly characteristic of cardiac decompensation and suggest a further cause for the dyspnea and cough. When treatment for congestive failure was given, the signs in the left chest cleared fairly well but the findings in the right chest were not improved.

The white-cell count was 43,000, with 90 per cent neutrophils and a marked shift to the left, which is suggestive of acute infection. One wonders if the patient had leukemia, but there is no indication that there were any really young cells or any enlargement of the lymph nodes, liver or spleen, although examination of the abdomen was rather difficult. I shall exclude that possibility and take the high white-cell count with the high percentage of neutrophils and the shift to the left as an indication of acute infection. In other words, I am inclined to think that an acute infectious process was going on in the chest, which was possibly an added complication to the existing cardiac condition.

As for the pulmonary infection, one wonders about bronchiectasis, with a history for a year. Opposed to that are the completely negative lung fields by x-ray study and the fact that five weeks before admission the sputum was not particularly characteristic. One wonders about carcinoma obstructing a bronchus, with infection beyond the obstruction. Again the negative x-ray findings argue against that possibility. With sudden and complete signs developing rather quickly, one wonders about lung abscess, which can be excluded, however the sputum was not characteristic, and there was no suggestion of the signs and symptoms that are apt to precede a lung abscess. One wonders about an infarct, but with an infarct that gave so many signs in the chest over such a large area one would expect bloody sputum and a more sudden collapse than this story implies. It is much more probable that this patient had beginning congestive failure, with a superimposed acute infection of the lungs — a pneumonitis of one sort or another — and, possibly, some fluid in the pleural space. I rather think that the pneumonia was the final straw that broke the camel's back.

That brings up the question of the heart lesion, whose nature depends somewhat on the findings given. For instance, we are told that five weeks before entry, on examination by an outside physician, an aortic diastolic murmur was recorded. Later, on admission to the hospital, no murmurs were heard. It is important to realize that at that time the record goes out of the way to say that the patient had a noisy chest and rapid pulse (140) and was in a critical state. A definite aortic diastolic murmur was probably heard when there was a good opportunity to listen to the heart under normal conditions. I therefore believe that the heart was enlarged, with aortic regurgitation.

When these facts are put together one is led to consider three main types of heart disease. The first is rheumatic heart disease, with aortic regurgitation, but such a lesion would probably have caused trouble before the age of sixty-five. One might suppose that the whole picture was explained by an acute attack of rheumatic fever, unusual but

still possible in older people, superimposed on an already damaged rheumatic heart, but such an explanation is unlikely statistically. The second type is hypertensive arteriosclerotic heart disease, in which aortic regurgitation is sometimes found with dilatation of the heart. To be sure, the patient had no hypertension during the time she was observed, but we know that such patients may have a low blood pressure when the heart begins to fail. I am inclined to discard that diagnosis because one finding suggests a third type of heart disease, namely, syphilitic heart disease. To be sure syphilitic heart disease is more usual in the forties and fifties, but it does occur in the sixties and seventies. It is about five times as frequent in men as in women. There are some things, however, in favor of syphilitic heart disease in this case. The patient had a cardiac condition that progressed to death in the course of a year from the time it was first noted or from the time of the first symptoms. She had an aortic diastolic murmur, which is consistent with syphilitic aortitis, and she died of cardiac asthma or pulmonary edema, which is a characteristic end in syphilitic heart disease. She also had unequal and irregular pupils. There is a definite association between central-nervous-system and cardiovascular syphilis. I believe that 10 to 20 per cent of the people with cardiovascular syphilis also have central-nervous-system syphilis. What the percentage is in the reverse situation, I do not know. I think that this patient had syphilitic heart disease, although we are not given the results of a blood Hinton test. Having decided that, one can ask whether an aneurysm developed and blocked off a bronchus to produce the chest findings. In view of the negative x-ray study for aneurysm five weeks before entry, it is too much to suppose that an aneurysm of these proportions would have developed within the short time before the patient entered the hospital. One can wonder about coronary closure, which occurs in syphilis at the mouth of the coronary artery, but preceding this attack of failure there was no history of pain and coronary closure is therefore unlikely.

I shall conclude by making the following diagnoses: syphilitic heart disease, with aortic regurgitation, cardiac decompensation, with pulmonary edema, right pleural effusion, possibly secondarily infected, pneumonitis in the right lower and middle lobes, and syphilis of the central nervous system.

DR WILLIAM D SMITH This patient was sent to me in my office almost five weeks before she came to the hospital. The history was interesting because the only complaint was cough, which was at first paroxysmal, occurred mostly in the morning and had grown steadily worse until, for two weeks, it had kept her awake almost all night, in spite of the fact that she was taking cough medicine, which her own physician had given her. Another interesting thing was that two months before admission she had

a wheeze, which persisted for two weeks and ended in a tremendous paroxysm of cough in which she raised a small hard mass of something that nobody could identify.

DR WALTER BAUER Was the wheeze bilateral?

DR SMITH I do not know about that. She said that about two months previously she wheezed almost constantly but the wheezing ceased after the coughing paroxysm, with the extrusion of the small hard lump. So far as the heart is concerned she had no failure at the time I saw her, although she did have a moderately enlarged heart. She had a systolic and an early blowing diastolic murmur at the apex. The heart rate was regular, and she had no signs of chronic passive congestion and never admitted any shortness of breath, except during the paroxysm of cough.

I could not find anything in the chest. She coughed a great deal in the office—it was a dry hard cough. We tried to get sputum and did get an infinitesimal amount of mucus. She had been checked two or three weeks earlier at another hospital, but in spite of the fact that she had had an x-ray examination three weeks before I saw her, I had another x-ray film taken, which was negative. Because of the hoarseness, which I supposed was due to chronic cough, I had a nose-and-throat man examine the larynx and trachea, which he reported showed only extreme redness. The blood pressure was within normal limits, and the urine was normal. My opinion was that, in addition to the heart that had given no symptoms, the patient almost surely had disease of the lung. I wanted her to come in to the hospital for further study, but she went to Philadelphia to visit her sister, and the next time that I heard from her, her physician telephoned that she was in cardiac failure, she was sent to the hospital in a moribund condition. I thought that she must have had some lung disease that had not been discovered. She had no pain in the chest and no hemoptysis.

DR BAUER She had an aortic murmur.

DR SMITH Yes. The heart was moderately enlarged. She had a systolic murmur at the apex and a rather faint but definite early aortic diastolic murmur, which I could hear at the apex much better than elsewhere.

DR GRAHAM I am impressed with the first-hand description of the cough. It seems to me to have been a much more prominent feature for a longer time than I had gathered from the record. I am also impressed by the fact that if it had been on a cardiac basis Dr Smith would have detected more evidence of cardiac failure at the time he saw the patient. The degree of cough is the most striking thing he described and raises the question whether this patient had adenoma of the bronchus, which did not show in the x-ray film but finally plugged the bronchus and gave rise to a secondary infectious process.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease, with congestive failure
 Pulmonary edema and right pleural effusion
 Bronchopneumonia, extensive

DR GRAHAM'S DIAGNOSES

Syphilitic heart disease, with aortic regurgitation
 Congestive heart failure
 Chronic pneumonitis, right
 Pleural effusion
 Central-nervous-system syphilis?

ANATOMICAL DIAGNOSES

Empyema, right.
 Lung abscess, right lower lobe
 Chronic pneumonitis, right lower lobe
 Broncholiths, with ulceration of right and left bronchi
 Tuberculosis, calcified, of bronchial lymph nodes
 Traction diverticulum of esophagus

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN Autopsy showed empyema of the right pleural cavity—1200 cc of foul-smelling purulent material. In removing most of this fluid we discovered that it had developed from a small abscess in the right lower lobe. The abscess was rather well defined, measuring 2 to 3 cm in diameter. Around the abscess, involving the greater part of the right lobe, was a chronic pneumonitis. The remaining lobes, which appeared perfectly normal, were not congested to any extent.

The interesting thing about this case is the cause of the lung abscess. Scattered over the mucosa of the

lower trachea and both bronchi were about five or six irregular foci of black anthracotic pigmentation. These areas were closely related to calcified anthracotic mediastinal lymph nodes adherent to the wall of the trachea and bronchi, and in each bronchus just beyond the carina a calcified node had eroded through the mucosa and presented in the lumen. The larger protruding calcified mass measured about 1 cm in diameter. We were unable to find a calcified mass in the abscess. Perhaps the mass that produced the abscess was the one the patient coughed up. I believe that the chronic pneumonitis and abscess originated from one of these so-called "broncholiths."

We were unable to find any evidence of active tuberculosis anywhere. There were scars at the apexes, evidence of old tuberculosis, and the regional nodes showed calcification. The calcified lymph nodes had also produced a traction diverticulum of the esophagus.

The heart was not remarkable; it weighed only 325 gm, the valves were normal, and coronary arteries showed extremely little sclerosis.

DR BAUER There was no evidence of valvular disease?

DR CASTLEMAN No.

A PHYSICIAN That does not explain the inequality of the pupils.

DR CASTLEMAN We did not examine the head.

It is strange that nothing was discovered in the right lower lobe when the patient was examined five weeks previously, because the pneumonitis was chronic. Many of the bronchi were plugged with connective tissue reminiscent of bronchiolitis fibrosa obliterans, and some of the small arteries in that region were plugged with thrombi such as one might see in an old infection.

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THE TREATMENT OF BACTERIAL MENINGITIS

THERE is a general impression among a great many physicians that the recent introduction of potent antibacterial agents, including the sulfa drugs and particularly penicillin, has rendered bacteriologic diagnosis unnecessary and obsolete. This impression is fostered and strengthened by the necessity for the early use of these agents to obtain the optimum effect in the treatment of infections and also by the fact that cultural results are so often meaningless if materials are obtained for examination after these forms of antibacterial therapy have been given for any length of time. The fallacies in this reasoning and the practical importance of early and proper bacteriologic diagnosis of infections prior to treatment with modern chemotherapeutic

and antibiotic agents are most strikingly illustrated in a group of the most serious infectious diseases, namely, the bacterial meningitides.

Elsewhere in this issue of the *Journal* there is a report of the treatment of 9 cases of *Haemophilus influenzae* meningitis. In 7 of these cases, cure of this infection was attributable solely to the use of the new antibiotic streptomycin. The results in these cases and the experience of others in similar cases seem to justify the conclusions that at the present time streptomycin is the best treatment for this type of meningitis and that the antibiotic should be given both intrathecally and intramuscularly.

Prior to the introduction of streptomycin, comparable results were obtained in cases of meningitis caused by Type B strains of *H. influenzae* by the use of specific rabbit antiserum supplemented by sulfonamides. This form of treatment should still be considered as a useful alternative when streptomycin is not available or when treatment with the antibiotic is not effective. The latter possibility may prove to be an important and serious one because the development of resistance or "fastness" during the course of treatment of infections due to organisms that were originally susceptible to streptomycin has already been encountered more frequently with this antibiotic than with any of the other antibacterial agents now in use.

Two of the 9 reported cases of *H. influenzae* meningitis were complicated by severe *Staphylococcus aureus* infections, which occurred after the patients were completely free of *H. influenzae*. It was necessary to resort to full doses of penicillin for the treatment of these staphylococcal infections and a cure was effected in one of the cases by such therapy. The fact that recovery would probably not have occurred without penicillin in this case is further proof of the usefulness of bacteriologic studies. The data derived from bacteriologic studies are therefore useful not only in determining the optimum therapy but also, together with the clinical findings, in helping to establish the causes of failure.

Thus it has been shown that meningococcal meningitis is best treated by parenteral or oral sulfonamides and that penicillin is probably unnecessary, although it may be used as an adjunct in severe bacteremic cases. Penicillin alone, even when

given parenterally and intrathecally, has frequently been found to be inferior to sulfonamides in cases of meningococcal meningitis. In cases of hemolytic streptococcus infection the sulfonamide drugs alone may also be adequate. In such cases, however, there seems to be more justification for the use of penicillin because of the marked sensitivity of most strains of hemolytic streptococci to penicillin and because of the recent increase in the number of sulfonamide-resistant strains of this organism. Cases of pneumococcal and staphylococcal meningitis require the combined use of sulfonamides and penicillin, the latter being given both parenterally and intrathecally. The necessity for this combined treatment is based on the reported results in clinical cases and also has some experimental basis. Meningitis due to gram-negative bacilli usually does not respond well to treatment with sulfonamides alone, and penicillin generally has no effect whatever in these cases. Streptomycin given parenterally and intrathecally offers the best hope in such cases, although proof of the value of this agent in meningitis is not yet available except in cases due to *H. influenzae*. The necessity for intrathecal therapy with streptomycin, as with penicillin, is based on the poor penetration of these antibiotics into the cerebrospinal fluid. The duration of treatment is also dependent on the causative agent and varies from a brief period of perhaps two or three days after sterilization of the spinal fluid in cases of meningococcal meningitis to as long as three weeks or even longer in cases of staphylococcal meningitis.

In addition to these pyogenic infections of the meninges, cases of syphilitic meningitis have now been shown to respond to treatment with penicillin. Parenteral therapy is adequate, intrathecal therapy not only being unnecessary but also often resulting in serious reactions. There is also one case of apparent recovery following systemic and intrathecal treatment with streptomycin in a proved case of tuberculous meningitis.*

The best practical procedure to be followed when one is confronted with a clinical case of meningitis is to obtain the materials for bacteriologic study as soon as the diagnosis is made or suspected. One

may then proceed immediately with therapy along the lines suggested by the likeliest clinical diagnosis. A change to the optimum treatment is then made after the etiologic diagnosis is established from the cultures of the blood or spinal fluid. The proper choice of antibacterial agent, dosage and route and duration of therapy, as well as the prognosis, all depend on the etiologic diagnosis. Further cultural studies are indicated in following the course of the infection, particularly when the response of the patient, as judged from the clinical and laboratory observations, seems inadequate.

THE FIRST DESCRIPTION OF RICKETS

Just over three hundred years ago, in 1645, a young man, formerly a student at Merton College, Oxford, finished a course of medicine at the University of Leyden and was given a medical degree. As usual, he was required to write a graduation thesis. This was read in Latin before his examiners at Leyden on October 18, 1645, by Daniel Whistler, then twenty-five years of age. In the title he used the English word "rickets," thus publishing for the first time, so far as is known, the name that the disease still bears. It is not quite clear where this name came from. Whistler stated that the disease had been observed in England for at least twenty-five years and that the name was said to have been taken from the surname of a quack who was the first to treat the condition. Others have pointed out that this fanciful name arose in the county of Dorset, where those who are short of breath are said, in the dialect of the district, "to rucket." Wherever the name originally came from, the addition of it to medical literature is due to the medical student, Daniel Whistler.

Whistler's description of the disease is a concise and clear statement of most of the then known facts and, according to Still,¹ appears to have been based on personal observations. As Whistler did no post-mortem examinations, his description of the pathology of rickets is purely speculative. Still believes that Whistler may have known of the incomplete description of rickets published by Reusner in 1582, but Whistler's description was almost certainly the result of personal contacts with patients and not

*Cooke, R. E., Dunphy, D. L., and Blake, F. G. Streptomycin in tuberculous meningitis: report of its use in one-year-old infant. *Yale J Biol & Med* 18:221-226, 1946.

imply the copying of material from a previous author

The thesis had little influence on the development of knowledge of this condition, for it was not until Francis Glisson and a committee of seven at the Royal College of Physicians in London investigated the disease and published their report in 1650 that rickets was accepted as a clinical entity

Whistler's later career was not a happy one After returning to London from Leyden, he received his medical degree at Oxford in 1647 and became a fellow of the College of Physicians two years later He then practiced medicine in London, but his interests were widespread since he taught geometry at Gresham College and served as a Linacre Reader at Oxford Whistler served as a naval surgeon and later traveled in Sweden Honored by being elected as the Harvey Orator in 1659, he ultimately rose to the office of treasurer and finally that of president of the College of Physicians Both Samuel Pepys and John Evelyn, the diarists, were friends

It was toward the end of his life that Daniel Whistler got into difficulties, and after his death Munk,² the historian of the Royal College of Physicians, wrote "Whistler's character will not bear examination, and it would have been well for the interest of the College had he not admitted to some, at least, of the places of trust he was elected to fill His manners were agreeable and he shone particularly in society, yet it is but too evident that duty, honor and probity weighed but lightly with him" He apparently handled the financial matters of the College of Physicians badly and probably misappropriated some of the funds He is said to have married a rich widow His extensive practice in London brought him in a thousand pounds a year, a large sum for the middle of the seventeenth century, and yet he died in debt, with a blot on his name, which cannot be erased even after three hundred years He should be remembered, however, for his account of rickets, which established the name of the disease, although at the time his medical thesis from the University of Leyden attracted little attention Whistler, no doubt, resented this, particularly since so much recognition had been given to Glisson, as a result he had his thesis reprinted in London in 1684, shortly before his death

REFERENCES

- 1 Sall G F *The History of Paediatrics The progress of the study of diseases of children up to the end of the XVIIIth century* 526 pp London Milford 1951
- 2 Munk W *The Roll of the Royal College of Physicians of London* 3 vol Second edition 1435 pp London Harrison & Son, 1878

MISCELLANY

NOTES

The following appointments to the teaching staff of Harvard Medical School have recently been announced Frank Dennette Adams, of Boston (Lit B Princeton University 1915, M.D. Harvard University 1917), instructor in medicine, Marshall Kinne Bartlett, of Dedham (A.B. Yale University 1924, M.D. Harvard University 1928), instructor in surgery, Joseph Henry Bragdon, of Milton (A.B. Yale University 1935, M.D. Columbia University 1939), instructor in pathology, Joseph Messer Clough, of New London, New Hampshire (A.B. Dartmouth College 1931, M.D. Jefferson Medical College 1936), assistant in ophthalmology, David Wesley Compton, of Vashon, Washington (S.B. University of Washington 1937, M.D. University of Pennsylvania 1941), assistant in anesthesia, Geoffrey Edsall, of Cambridge (M.D. Harvard University 1934), instructor in bacteriology and immunology, Milton Elkin, of Andover (A.B. Harvard University 1937), M.D. Harvard University 1941, assistant in medicine, Robert Goldstein, of Dover, New Jersey (A.B. Princeton 1935, M.D. Harvard University 1937), assistant in medicine, James Hutcheson Graham, of Westmount, Quebec (M.D.C.M. McGill University 1942), assistant in medicine, William Frederick Greenwood, of Toronto, Ontario (M.D. University of Toronto 1937), research fellow in physiology, Lorne Edward Hackworth, of Sheffield, Alabama (S.B. Florence, Alabama, State Teachers College 1936, S.M. University of Alabama 1938, M.D. Harvard University 1945), assistant and Arthur Tracy Cabot Fellow in Surgery, George Kelemen, of Boston (M.D. University of Budapest 1915), instructor in otology, Wiland Fenway Leadbetter, of Needham (S.B. Bates College 1928, M.D. Johns Hopkins University 1932), assistant in genitourinary surgery, Arthur Paige Long, of Needham (S.B. University of Iowa 1932, M.D. University of Iowa 1934, M.P.H. Harvard University 1937, D.P.H. Harvard University 1938), instructor in bacteriology and immunology, Charles Pearson Lyman, of Brookline (A.B. Harvard University, 1936, A.M. Harvard University 1939, Ph.D. Harvard University 1942), research fellow in anatomy, Alexander Marble, of Boston (A.B. University of Kansas, 1922, A.M. University of Kansas 1923, M.D. Harvard University 1927), instructor in medicine, Edward Meilman, of Roxbury (A.B. Harvard University 1936, M.D. Harvard University 1940), assistant in medicine, Tom Fite Paine, Jr., of Aberdeen, Mississippi (S.B. Vanderbilt University 1939, M.D. Vanderbilt University 1942), research fellow in medicine, George Pike, of Roxbury (A.B. Harvard University 1932, M.D. Harvard University 1936), assistant in medicine, Eugene Edwin Record, of Boston (S.B. Harvard University 1932, M.D. McGill University 1937), assistant in orthopedic surgery, Carter Redd Rowe, of Fredericksburg, Virginia (A.B. Davidson College 1928, M.D. Harvard University 1935), assistant in orthopedic surgery, Earl Spinks Scale, of Boston (M.D. Tulane University 1935), assistant in ophthalmology, Gerald Shortz, of Kendallville, Indiana (S.B. Indiana University 1934, M.D. Indiana University 1936), assistant in anesthesia, Francis Marott Sinex, of Indianapolis, Indiana (A.B. DePauw University 1943, A.M. Indiana University 1944), teaching fellow in biological chemistry, Arthur Kaskel Solomon, of Cambridge (A.B. Princeton University 1934, A.M. Harvard University 1935, Ph.D. Harvard University 1937), assistant professor of physical chemistry, Howard Ingram Suby, of Newton Center (A.B. University of Wisconsin 1930, M.D. Harvard University 1934), assistant in genitourinary surgery, James Joseph Thomas, of Alliance, Ohio (S.B. Mount Union College 1935, M.D. Ohio State University 1940), assistant in anesthesia, Arthur Wallace Tucker, Jr., of Needham (A.B. Dartmouth College 1937, M.D. Harvard University 1941), assistant in obstetrics,

and William Anthony Weiss, of Philadelphia, Pennsylvania (S B Georgetown University 1934, M D Jefferson Medical College 1938), assistant in anesthesia

The College of Physicians of Philadelphia awarded the Alvarenga Prize on July 14, 1946, to Dr William H Feldman, of the Mayo Foundation for Medical Education and Research, in recognition of his studies on chemotherapy in tuberculosis

The Alvarenga Prize was established by the will of Pedro Francisco daCosta Alvarenga, of Lisbon, Portugal, an associate fellow of the College of Physicians, to be awarded annually by the College of Physicians on each anniversary of the death of the testator, July 14, 1883, to the author of a memorial on any branch of and line that is deemed worthy of the prize

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request

Dietotherapy Clinical application of modern nutrition Edited by Michael G Wohl, M D, associate professor of medicine, Temple University School of Medicine, and chairman, Advisory Committee on Nutrition, Philadelphia Department of Public Health. With a foreword by Russell M Wilder, M D, Ph D, professor of medicine and chief of the Department of Medicine, Mayo Foundation, and member of the Committee on Medicine and of the Subcommittee on Medical Nutrition, Division of Medical Sciences, National Research Council. 8°, cloth, 1029 pp, with 93 illustrations. Philadelphia W B Saunders Company, 1945 \$10.00

This new treatise on nutrition in health and disease is a composite work of fifty-eight recognized authorities in various fields of medicine. The objective of the book is to provide the practicing physician and the student of medicine with the sound knowledge of current advances in and practical applications of the rapidly expanding science of nutrition. The subject matter is divided into three parts: normal nutrition, nutrition in periods of physiologic stress and nutrition in disease. Selected lists of references are appended to each chapter.

Preventive Medicine By Mark F Boyd, M D, C P H, field staff member, International Health Division, Rockefeller Foundation. Seventh edition, revised. 8°, cloth, 591 pp, with 187 illustrations and 56 tables. Philadelphia W B Saunders Company, 1945 \$5.50

This standard text has been thoroughly revised and brought up to date. New material has been added, and many divisions have been expanded, rearranged and rewritten. The section dealing with nutrition has been entirely recast in the light of current concepts. Rheumatic fever, leptospirosis and asbestosis are included for the first time. The work is recommended for all medical libraries.

Technical Methods for the Technician By Anson L Brown, M D, director of Dr Brown's Clinical Laboratory and Dr Brown's School for Technicians, Columbus, Ohio. Third edition. 8°, cloth, 707 pp, with 229 illustrations. Columbus, Ohio B B Printing Company, 1944

This standard text written for students and clinical laboratory workers has been thoroughly revised. Many new methods and procedures have been added to the text. The emphasis is on technique, but interpretations are given for most procedures. In this edition new illustrations and colored plates have been added. In the section on serology the author's test for syphilis is presented for the first time. The author concludes his work with a list of one hundred and five standard laboratory reference books. This book should prove valuable to all laboratory workers and serve as a reference source in medical libraries.

Diseases of the Nervous System in Infancy, Childhood and Adolescence By Frank R Ford, M D, associate professor of neurology, Johns Hopkins University. Second edition. 4°, cloth, 1143 pp, with 164 illustrations. Springfield, Illinois Charles C Thomas, 1944 \$12.50

In this second edition of an authoritative text the many errors of the first edition have been corrected and the author has taken advantage of the helpful criticisms offered to him. Select bibliographies are appended to each disease, and the text is amplified by many pertinent case histories. The book is well printed, with a good type, on good paper and is recommended for all medical libraries and to all those interested in the diseases of the nervous system.

Public Medical Care Principles and problems By Franz Goldmann, M D. 8°, cloth, 226 pp. New York Columbia University Press, 1945 \$2.75

In this book Dr Goldmann attempts to give a composite picture of public medical care as a social movement. He deals with community health activities supported by taxation and administered by governmental agencies. In the first part, after a review of the history of public medical care, the author analyzes, interprets and appraises public policy in providing facilities and services for the care of the sick. In the second part he discusses the problem of planning for medical care and shows the potential value of the method of taxation to the development of broad programs of health and social security in the future.

The Autobiography of Science Edited by Forest R Moulton, Ph D, Sc D, and Justus J Schifferes. 8°, cloth, 666 pp. Garden City, New York Doubleday, Doran and Company, Incorporated. \$4.00

The editors of this new history of science have attempted to provide an anthology of the key passages from the master works of all sciences. The selections are in general arranged in chronological order from the time of genesis to modern times. Medicine is well represented in the selections, and this book should be in all historical collections.

Pulmonary Tuberculosis in the Adult Its fundamental aspects By Max Pinner, M D, chief, Division of Pulmonary Diseases, Montefiore Hospital for Chronic Diseases, New York City, and clinical professor of medicine, College of Physicians and Surgeons, Columbia University. 8°, cloth, 579 pp, with 59 illustrations and 3 graphs. Springfield, Illinois Charles C Thomas, 1945 \$7.50

This new work on pulmonary tuberculosis considers the subject in all its phases as interrelated to each other. Extensive bibliographies are appended to each chapter, and each reference is annotated, a new and time-saving feature in bibliographies.

NOTICES

ANNOUNCEMENTS

Dr Marcus W Berman, having returned from military service, announces the opening of his office for the practice of medicine and surgery at 304 Belgrade Avenue, Roshardsle

Dr Sydney Grace, having returned from military service, announces the reopening of his office at 311 Commonwealth Avenue, Boston, for the practice of obstetrics and gynecology

Dr Sidney Olans, having returned from active service with the Army, announces the reopening of his office for the practice of medicine and obstetrics at 20 Intervale Avenue, Medford

Dr Robert H Talkov has returned from military service and will resume the practice of internal medicine with special interest in arthritis and allied rheumatic disease at 375 Commonwealth Avenue, Boston

(Notices continued on page xvi)

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INFECTIOUS HEPATITIS IN MASSACHUSETTS

With a Review of Present Knowledge of the Disease

HARRIET L. HARDY, M.D.,* AND ROY FEEMSTER, M.D.†

BOSTON

THE recent literature describing the experience of the armed forces with infectious hepatitis is voluminous, but reports on the disease in the civilian population have been few. This article summarizes our present knowledge of the disease and indicates how nearly our observations coincide with or differ from those of others. The clinical material used as the basis of this paper has been collected by means of visits to Massachusetts communities from which the disease has been informally reported to the Department of Public Health. Approximately 175 cases of infectious hepatitis were uncovered in Massachusetts in these investigations, but only 151 case histories are used in this report, since in the remaining cases 24 insufficient data were available to make their analysis reliable.

A short explanation of nomenclature in this disease will be useful. "Epidemic catarrhal jaundice" and "nonspirochetal infectious jaundice" are the terms that have been used in the past to designate it. "Infectious hepatic jaundice" appeared as a title in 1937, when it was realized that the infection is localized in the liver rather than in the duodenum and larger bile ducts. At present the term "infectious hepatitis" — or with English authors "infective hepatitis" — is used to designate sporadic cases and "infectious epidemic hepatitis" for groups of cases during outbreaks. An occasional writer refers to infectious hepatitis as "hepatocellular catarrhal icterus";^{2,3} a term of doubtful value.

The limits of this discussion make it impossible to do more than mention the vast store of accumulating facts concerning artificially acquired hepatitis, which is in many ways identical with naturally acquired infectious hepatitis. Oliphant⁴ has shown that the causative organism of infectious hepatitis is present in an infective state in the blood of patients with this disease.

The term "homologous serum jaundice" is used to refer to hepatitis artificially acquired from any cause. The clinical picture produced by this condition is similar to that observed in infectious epidemic hepatitis.⁵⁻⁸ The incubation period is different in the two diseases.⁹⁻¹¹ An attack of homologous serum jaundice does not protect against infectious epidemic hepatitis.^{9,12} It may be that there are separate etiologic agents for the two diseases.

At the present time, artificially acquired hepatitis appearing from a variety of sources is classified as homologous serum jaundice. Reports show that this disease has occurred after the use of certain lots of yellow-fever vaccine,^{5,13-17} measles antiserum,^{18,19} and mumps convalescent serum.^{20,21} Hepatitis after transfusion,^{7,14,19,22} is now a well recognized occurrence. Contamination of syringes by infected serum has been reported both from a diabetic clinic²³ and following the administration of anti-syphilitic arsphenamine.²⁴⁻²⁶

HISTORY

The available medical literature contains many statements concerning jaundice of a contagious variety. Hippocrates knew and wrote of such a disease.²⁷ Letters between Pope Zacharias and St. Boniface in the eighth century A.D.²⁸ describe epidemics of jaundice. The American Civil War produced many cases of a disabling, highly contagious jaundice.²⁹ Pomeroy³⁰ in 1898 in Michigan and Leslie³¹ in 1909 in Maine described outbreaks much like the one to be discussed herein. Cockayne²⁷ in 1912 in England wrote an impressive and complete report of the information and literature then available. His article contains speculation that is now known to be based on facts.

Much was written after the British had had experience with huge numbers of men sick with jaundice at Gallipoli and the Dardanelles in 1915-1916.³²⁻³⁶ From these reports it is apparent that

*Assistant district health officer, Massachusetts Department of Public Health; assistant in medicine, Massachusetts General Hospital.

†Director, Division of Communicable Diseases, Massachusetts Department of Public Health.

Weil's disease was not yet understood Willcox³⁶ in 1919 made a clear classification and separated epidemic catarrhal jaundice from other forms of contagious and noncontagious jaundice³⁷⁻⁴⁷ American observers showed an interest in outbreaks of jaundice, especially Williams,⁴⁸ Wadsworth⁴⁴ and Symmers⁴⁹ in New York State, Hiscock and Rogers⁴⁹ in Connecticut described its occurrence among college students in 1922 Blumer⁵⁰ presented an extensive study of what he called infectious jaundice in the United States in 1923 In that same year, Jones and Minot⁵¹ published a careful clinical estimate of the disease, pleading for more attention to its extent and potential dangers The English literature of the 1930's⁵²⁻⁵⁹ contains scattered reports of outbreaks, as does the literature of other countries,⁶⁰⁻⁷⁰ with a few American records^{71, 72}

One cannot be certain that all these outbreaks belonged in a single group, since the etiologic agent had not been discovered, but there does appear to be a basic pattern in the histories of such episodes Since the outbreak of hostilities in the Mediterranean theater, the German,⁷³⁻⁷⁵ Italian,⁷⁶ French,⁷⁷ British⁷⁸⁻⁸⁰ and American armies,^{81, 82} as well as refugees in Palestine,⁸³⁻⁸⁵ have suffered serious morbidity from infectious hepatitis The Navy has by no means escaped⁸⁶⁻⁸⁸

ETIOLOGIC AGENT

It is now held that infectious hepatitis is caused by a specific virus This virus has not yet been grown in the laboratory Swedish investigators⁸⁹ in 1938 believed that they had successfully infected swine with the causative agent of infectious hepatitis This has not been confirmed German authors^{90, 91} claimed to have been able to make the organism grow in the chorioallantoic membrane of chicks Other German workers⁹² claimed that the organism could be passed to birds This work is not convincing and has not been repeated Cameron⁹³ and Van Rooyen and Gordon⁹⁴ tried without success to infect animals during their experience in the Middle East Hovle⁹⁵ in England tried every possible route in mice, guinea pigs and chick embryos but was equally unsuccessful Paul and his group¹² have tried all the animals named, as well as monkeys, but have not been able to produce infectious hepatitis in any of them

It has been possible to transmit infectious hepatitis to human volunteers This has been done in England¹⁰ and America¹² It is now known that human volunteers can develop the disease following the parenteral injection of small amounts of infective serum,^{4, 9} following ingestion of infective serum or feces¹⁰ and following the spraying of infective feces into the nasopharyngeal passages¹² Certain facts about the virus itself are also known Havens⁹⁶ has shown it to be extremely resistant to heat and capable of passing through the finest filters MacCallum and Bradley¹⁰ have demonstrated that the

organism remains actively infective after drying and after storage in the dried state up to fourteen months Stokes et al⁹⁷ have suggested that chlorination of water contaminated with the virus of infectious hepatitis attenuates but does not kill the organism The virus may prove to be resistant to chemicals in the strengths in which they are ordinarily used for the purification of water

EPIDEMIOLOGY

Age

Reports lead one to believe that infectious hepatitis, like other contagious diseases, may attack persons of any age^{46, 50, 55-57, 85, 98-100} The age distribution of the 151 cases collected in Massachusetts was as follows under five years, 8.6 per cent, five to nine, 17.2 per cent, ten to fourteen, 17.9 per cent, fifteen to nineteen, 11.9 per cent, twenty to twenty-four, 6.7 per cent, twenty-five to twenty-nine, 9.3 per cent, thirty to thirty-four, 11.2 per cent, thirty-five to thirty-nine, 9.3 per cent, and over forty, 8.0 per cent Persons between six and forty years of age are oftenest affected The authors reporting on special age groups, such as college students^{49, 101} and soldiers,^{75, 80, 102-104} do not, of course, have a wide range, but health officers in England^{55, 105} and physicians in rural communities in America^{31, 50, 106} show a wider distribution of ages affected Our observations in Massachusetts in 1945 suggest that different age groups are preponderantly affected in different communities within a single outbreak period Community A in Massachusetts, for instance, showed a higher rate among young adults, although the population was not preponderantly of any particular age group, whereas Community C showed a far greater incidence among the children of early school age (six to ten years), in spite of the fact that adolescents and young adults were heavily exposed at school and in the home Chance or the operation of unknown laws of susceptibility must account for this variation

Sex

The disease affects both sexes practically equally In our series, there were 71 males and 80 females

Geographical Distribution

There is no question that infectious hepatitis has a world-wide distribution For the reader's interest, references to a number of epidemics believed to belong under the heading of epidemic infectious hepatitis are cited^{27, 28, 32, 35, 37, 42, 43, 47, 50-53, 55-70, 76, 77, 107}

Incidence

According to the records, the incidence of infectious hepatitis has varied enormously A workable concept is that this disease, like poliomyelitis, is always present in the form of sporadic cases Epidemics take place from time to time and in various regions when natural conditions favor the growth of the virus and when artificial conditions of crowding

and poor conditions of all sorts exist. In 1898, Pomeroy³⁰ reported 676 cases among 30,000 persons in Michigan. Williams⁴⁸ reports 700 cases in the 1921 outbreak in New York State and considers this to be about 50 per cent of the known cases. Pickles⁵² describes 250 cases in 5700 persons exposed. Rogers¹⁰¹ states that the average number of cases at Yale University in a nonepidemic year is 22, and in an epidemic year he reports 63 cases within fifteen days.

Stowman¹⁰⁸ refers to infectious hepatitis as the "new disease" of World War II, without giving supportive evidence of its newness. The disease is reportable in the Scandinavian countries, Finland and Switzerland, these countries reported 65,000 cases in 1943. Army experience^{80, 82, 109} is cited to give an idea of the extensiveness of the disease at present. The Navy⁸⁶⁻⁸⁸ in the South Pacific reports infectious hepatitis, as have the German,^{73, 75} Italian⁷⁶ and French⁷⁷ armies. Since the disease is reportable in only a few states in this country, we have no idea of its incidence. Blumer¹¹⁰ writes that it is reportable in California and that 118 cases were reported in 1943 and 335 in 1944. Handy¹⁰⁶ encountered well over 100 cases in a small New Hampshire community of 2500 persons between October, 1944, and April, 1945. Between May and July, 1945, we encountered reports of 175 cases in Massachusetts.

Season

In this small series, patients had onsets in every month, the lowest number being 9 in August and December and the highest, 80 in April^{25, 30, 50-55, 70, 75, 78, 85, 101-103, 111}

Immunity

Only speculation is possible concerning immunity following infectious hepatitis until a means is developed of determining whether a subject is having or has had the disease. The fact that the gamma globulin of blood pools apparently contains antibodies against infectious hepatitis¹¹² is suggestive of permanent immunity after an attack. Furthermore, the age group attacked—six to forty years—suggests that older persons have acquired immunity by a previous attack. A physician who has been in practice in the same community for over forty years recalls a series of cases that he attended thirty-one years ago that were identical in every way with those existing in 1945 in the same community. In only 1 case in our series was there a second attack. A woman teacher of forty-two years sick with the disease in 1945 gave a clear history of having had a similar clinical picture at sixteen years of age after exposure during an epidemic of so-called "yellow jaundice" in her schoolroom.

Period of Infectivity

Because of the epidemic possibilities of infectious hepatitis, it is important to know the period

of infectivity. Bates⁵⁹ considered the period to be four weeks after the onset of jaundice, and Pickles⁵² estimated it as eight days before and up to two weeks after onset. Pickles remarked that the period of infectivity must be short, because of his observation that new cases came at regular thirty-day intervals. It is now known from transmission experiments that blood serum and feces are infectious during the active stages of the disease.⁴³ More evidence on this point is accumulating.

Incubation Period

Transmission experiments prove that under controlled conditions the incubation period of infectious hepatitis is about thirty days.^{10, 12} Reports of epidemics suggest that many factors determine the time between cases in uncontrolled environments. Cockayne²⁷ and Glover⁵⁶ put the period between cases as four days, Pickles⁵² puts it at thirty-five days. Rogers¹⁰¹ states that the period of incubation for his cases was three to nineteen days, with an average of seven. Cameron⁸³ estimates the time as one to six months.

In our observation in Massachusetts in 1945, the period between cases in a household varied so widely that there scarcely seemed to be a pattern. In one family, 3 children became ill within six days at two-day intervals, in another family there were eight days, fourteen days, twenty-two days and twenty-eight days between the 4 cases. In two families living in adjoining homes, there were 3 cases in one house and 2 in another, and between each case there was a two-month interval, except in the last case, in which there was a twenty-one-day interval after probable exposure. The shorter periods apparently represent infection from the same source with variation in dates of onset, the longer ones may represent incubation periods of secondary cases. Because the virus is hardy⁹⁶ and may survive in the environment as well as in the body of the patient or carrier, it is often difficult to trace the source of infection and thereby determine the day of exposure. It is our impression that many factors influence the rapidity with which the virus produces symptoms. Such factors are undoubtedly responsible for some of the variation in the length of the incubation period. Stokes's⁹⁷ work with chemical alteration of the virus leads one to speculate that the incubation period may be lengthened by unknown factors affecting the virulence of the causative organism.

Method of Transmission

The important question of the method of transmission has not yet been settled. Although it is difficult to trace cases to contact with other known cases, the fact that cases occur in groups points to person-to-person contact as a method of spread. In our own series, contact of patients with probably infected groups was recorded in 139 cases, leaving only 12 sporadic cases in which no such association

Weil's disease was not yet understood Willcox³⁸ in 1919 made a clear classification and separated epidemic catarrhal jaundice from other forms of contagious and noncontagious jaundice³⁷⁻⁴⁷ American observers showed an interest in outbreaks of jaundice, especially Williams,⁴⁸ Wadsworth⁴⁴ and Symmers⁴⁰ in New York State, Hiscock and Rogers⁴⁶ in Connecticut described its occurrence among college students in 1922 Blumer⁵⁰ presented an extensive study of what he called infectious jaundice in the United States in 1923 In that same year, Jones and Minot⁵¹ published a careful clinical estimate of the disease, pleading for more attention to its extent and potential dangers The English literature of the 1930's⁵²⁻⁵⁹ contains scattered reports of outbreaks, as does the literature of other countries,⁶⁰⁻⁷⁰ with a few American records^{71, 72}

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EPIDEMIOLOGY

Age

Reports lead one to believe that infectious hepatitis, like other contagious diseases, may attack persons of any age^{46, 50, 55-57, 85, 98-100} The age distribution of the 151 cases collected in Massachusetts was as follows under five years, 8.6 per cent, five to nine, 17.2 per cent, ten to fourteen, 17.9 per cent, fifteen to nineteen, 11.9 per cent, twenty to twenty-four, 6.7 per cent, twenty-five to twenty-nine, 9.3 per cent, thirty to thirty-four, 11.2 per cent, thirty-five to thirty-nine, 9.3 per cent, and over forty, 8.0 per cent Persons between six and forty years of age are oftenest affected The authors reporting on special age groups, such as college students^{49, 101} and soldiers,^{75, 80, 102-104} do not, of course, have a wide range, but health officers in England^{55, 105} and physicians in rural communities in America^{31, 50, 106} show a wider distribution of ages affected Our observations in Massachusetts in 1945 suggest that different age groups are preponderantly affected in different communities within a single outbreak period Community A in Massachusetts, for instance, showed a higher rate among young adults, although the population was not preponderantly of any particular age group, whereas Community C showed a far greater incidence among the children of early school age (six to ten years), in spite of the fact that adolescents and young adults were heavily exposed at school and in the home Chance or the operation of unknown laws of susceptibility must account for this variation

Sex

The disease affects both sexes practically equally. In our series, there were 71 males and 80 females

Geographical Distribution

There is no question that infectious hepatitis has a world-wide distribution For the reader's interest, references to a number of epidemics believed to belong under the heading of epidemic infectious hepatitis are cited^{27, 28, 32, 35, 37, 42, 43, 47, 50-53, 55-70, 75, 77, 107}

Incidence

According to the records, the incidence of infectious hepatitis has varied enormously A workable concept is that this disease, like poliomyelitis, is always present in the form of sporadic cases Epidemics take place from time to time and in various regions when natural conditions favor the growth of the virus and when artificial conditions of crowding

further show that the excreta from such volunteer patients and from patients in the preicteric phase of infectious hepatitis will, if fed to susceptible persons, cause the disease, so that it seems more than likely that nonicteric cases exist, as observers have insisted. Their presence would help to explain the spread of the disease when it has not been possible to show contact. In view of their probable existence, it may not be necessary to postulate healthy carriers. Physicians whom we consulted commented on the unusual incidence of nonspecific vomiting and diarrhea in their experience during the past months, and one report¹¹⁸ is suggestive. Housewives spontaneously reported the same occurrence in their homes and those of their neighbors coincident with infectious hepatitis. There may well be some relation that will become clear when the behavior of the virus of this disease is understood.

PATHOLOGY

Infectious hepatitis, or catarrhal jaundice as the disease was named until recently in this country, has been held to be an inflammatory process causing edema in the large bile ducts and the duodenum, thus accounting for jaundice and other evidence of obstruction to the normal excretion of bile pigment.¹¹⁹ Cockayne²⁷ in 1912 pointed accurately to the relation between the disease and acute yellow atrophy. He suggested that a weakened liver made it simpler for the virus to attack that organ. In the years following this, the concept of catarrhal inflammation held sway. Throughout, some observers held the liver to be the site of disease. Jones and Minot¹²⁰ in 1923 brought out clinical evidence that pointed to the liver as the site of infection. Blumer,⁵⁰ also in 1923, reported a pathologist's finding in Buffalo, New York, to the effect that in 1921 there was more acute yellow atrophy than he had ever seen in one year. There was simultaneously a widespread outbreak of epidemic jaundice, as it was called. Experimental work by Humsforth and Glynn¹²¹ is relevant to the present concept of the pathologic physiology of infectious hepatitis.

Knowledge of the pathologic process has recently become more certain.¹²²⁻¹²⁴ The needle biopsy^{125, 126} has been introduced and in time, according to reports, will prove a reasonable diagnostic procedure for widespread use. Dible¹²⁷ has reported, after considerable experience, that most cases are pathologically benign and that following recovery no changes in the liver cells are visible. A small group of his patients showed mild but definite residual zonal fibrosis. Another small group showed classic cirrhosis as an end result. The fatal cases show acute and subacute hepatic necrosis of all grades of severity. The present view is that the virus causes damage in the hepatic cells themselves and that the clinical picture of obstruction depends on the inability of the cells to handle the bile pigment.

Lucké¹²⁸ has presented in detail the autopsy findings in 125 fatal cases of probable infectious hepatitis. These cases occurred among men in the armed forces. The livers in all cases showed parenchymal cell damage of all degrees, ending in acute yellow atrophy. In 75 per cent of the cases the spleen showed hyperplastic changes. Some of the kidneys showed cholemic nephrosis. In a moderate number of cases, there was edema of the brain and a meningo-encephalitis. Lucké mentions phlegmon of the intestinal tract. Lesions in the gastric mucosa of patients moderately ill with infectious hepatitis have been seen with the gastroscope.¹²³ Lucké's presentation suggests that infectious hepatitis may cause widespread damage in the body.

CLINICAL CHARACTERISTICS

This report on infectious hepatitis is based on histories obtained from hospitals and physicians, supplemented by talks with the patients themselves. Of the 151 patients, 22 were cared for in the hospital and 129 in their homes. These cases have been classified as 117 undeniable cases of infectious hepatitis and 34 likely cases. The former patients presented a history of contact, a convincing clinical picture and jaundice, whereas the latter gave a history of contact and a medical history characteristic of infectious hepatitis but no visible jaundice. All these patients came from communities in which the disease existed in sufficient numbers to give acceptable epidemiologic ground for considering the presence of infectious hepatitis to be epidemic in character.

Character of Onset

The onsets presented varying pictures in length and character. There were 31 cases of grippelike onset and 52 cases of abrupt or gradual onset, presenting chiefly gastrointestinal symptoms. Seventeen patients complained bitterly of abdominal pain at the onset; 5 of these localized their pains specifically in the right lower quadrant of the abdomen, and in 3 of these cases appendectomy was performed, 10 patients complained of severe headache, and 7 of some backache at the onset. Twenty-two mothers spoke of apathy, listlessness and drowsiness on the part of their children at this stage. A striking feature was that the onsets varied from community to community, suggesting that the strain of the virus may vary from one location to another. In Community A, the onsets were largely gastrointestinal in character, in Community B and Community D, grippelike onsets with inflamed throats led physicians to think of disease of the respiratory tract. In Community C, we encountered histories of headache, sleepiness and apathy as characteristic of the onset. A diagnosis of poliomyelitis, a not unknown occurrence,^{129, 130} was considered in 1 case.

The length of onset varied from a few days in 46 cases to two weeks in 16 cases and four weeks and

could be found. The kind of contact is shown in Table 1.

Blumer⁵⁰ made a similar classification.

From Table 2 it does not appear that a "clean" home is a guarantee that infectious hepatitis will not gain a foothold. It will be noted, however, that there is a preponderance of single cases in these homes. The same observation was made in regard

TABLE 1 *Nature of Contact*

PLACE	FAMILY CONTACT	SCHOOL CONTACT	JOB CONTACT	MISCELLANEOUS GROUP CONTACTS (PARTY MEETING)
Community A	33	8	15	6
Community B	4	11	0	1
Community C	13	14	2	1
Community D	6	7	1	1
Totals	56	40	18	9

to communities. Community A was suburban and prosperous, the homes were well kept, and the persons involved were for the most part conscious of sound health practice. Communities B and D were rural and less economically favored, the homes were less well cared for, and considerable ignorance and opposition to such public-health measures as milk pasteurization were encountered. Community C

TABLE 2 *Number of Cases Occurring in "Dirty" and "Clean" Homes*

	NO OF CASES IN HOUSEHOLD		NO OF HOUSEHOLDS	
			"DIRTY"	"CLEAN"
1			6	20
2			3	5
3			3	4
4			4	2
5			2	+0
6			1	+0
Totals			19	31

fell between, with a portion of both groups described. From Table 1 it appears that infectious hepatitis is independent of anything but the presence of the virus in the community, together with probable likely contact in the majority of cases, and individual susceptibility, since obviously not all those exposed in the six-to-forty-year group became ill.

Some of the possible methods of transmission discussed in the literature should be noted.

Insects. Two observers^{75, 104} thought that flies were important. Another writer¹⁰³ suggested bedbugs. The presence of infectious hepatitis at all seasons seems proof that except in rare instances of extremely bad sanitation insects are unimportant.

Fomites. There are no data that either prove or disprove the importance of contaminated articles. Since the virus is resistant to heat and chemicals,⁹⁸ infectious hepatitis may be transmitted by fomites.

Suggestive circumstances are found in the fact that 2 of the patients with infectious hepatitis in our series were postmen who handled letters coming from a theater of war known to be heavily infected with the disease. We learned also of a woman with infectious hepatitis who in previous months had received daily letters from her son, who was sick in Italy with the disease.

Water. There are three reports dealing with water as the vehicle for the virus of infectious hepatitis. Fraser⁵⁴ in Canada believed that his epidemiologic observations, together with proved fecal contamination of the water supply, showed an epidemic of infectious hepatitis to have been water-borne. Hallgren^{113, 114} in Sweden worked out a similar theory when an explosive outbreak appeared in an institution and a nearby village, both of which used water from the same contaminated reservoir. Neefe and Stokes¹¹⁵ claim that an outbreak in a girls' camp was due to contamination of a well by the feces of a patient with infectious hepatitis introduced into the camp early in the season. They produced sickness simulating infectious hepatitis in one of a group of volunteers by feeding them water from the supposedly contaminated well in the camp.¹¹⁶ Water seemed unimportant in our study, since there were multiple sources of drinking water, none of them convincingly contaminated. Cockayne⁹⁷ believed that water was ruled out by the evidence of infectious hepatitis in troops who were forbidden water and were given only tea to drink, yet among whom cases continued to appear.

Food. Rogers⁴⁹ and Blumer⁵⁰ thought that food might be the vehicle for the causative agent of infectious hepatitis. It appears certain that food-borne outbreaks have occurred in the past, because transmission experiments with volunteers have shown that the feces of active cases contain the virus of infectious hepatitis.¹²

Air. This has been the favorite explanation over the years.^{27, 30, 55, 58, 59, 100, 116, 117} From early concepts of bad air and vapors to the concept of droplet infection through talking, coughing and sneezing, most observers urged this theory even before the presence of a specific virus was demonstrated. In our study, droplet infection has seemed an important method of transmission because of contact between cases without the sharing of food or water.

In summary, study of the literature and observation of 151 cases of infectious hepatitis in Massachusetts in 1944-1945 led us to conclude that the disease is probably transmitted in more than one way — by droplet infection, by contaminated food and perhaps by water.

The possibility that nonicteric patients are potential carriers is still unexplored. Until a definite way of making a diagnosis has been developed, the existence of such cases can only be a subject of speculation. Work with volunteers shows that there are undoubtedly nonicteric cases.^{10, 12} These studies

further show that the excreta from such volunteer patients and from patients in the preicteric phase of infectious hepatitis will, if fed to susceptible persons, cause the disease, so that it seems more than likely that nonicteric cases exist, as observers have insisted. Their presence would help to explain the spread of the disease when it has not been possible to show contact. In view of their probable existence, it may not be necessary to postulate healthy carriers. Physicians whom we consulted commented on the unusual incidence of nonspecific vomiting and diarrhea in their experience during the past months, and one report¹¹⁸ is suggestive. Housewives spontaneously reported the same occurrence in their homes and those of their neighbors coincident with infectious hepatitis. There may well be some relation that will become clear when the behavior of the virus of this disease is understood.

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over in 4 cases Handy¹⁰⁶ had a similar experience in 1945 in New Hampshire. He reported caring for patients who felt ill and had vague gastrointestinal complaints for two months, suggesting the possibility of peptic ulcer. We have collected similar histories. Eventually such patients developed the usual picture of infectious hepatitis. These observations go far toward explaining the reports of widely varying incubation periods. With long, vague onset periods, depending to a degree on the subjective reaction of the patient, and with many patients ill with infectious hepatitis who never seek medical advice, the incubation period and period of onset cannot be definitely described during an outbreak in general medical practice.

Precipitating Factors

Factors apparently operating to precipitate infectious hepatitis were striking. These may account for the apparent susceptibility of one or two persons exposed to the same degree as the other members within a family or the other pupils in a school-room. There are reports of dysentery,^{33, 36, 111, 121-123} paratyphoid fever,³² chilling,^{31, 36, 102} respiratory infection^{27, 48, 55, 59, 101} and alcoholic excesses^{35, 80} as antecedent and important factors in outbreaks of infectious hepatitis in institutions and troops.

There were 44 cases of precipitating factors in this series. These included 10 cases of previous recent bacterial infection, 8 of a moderately large intake of alcohol, 15 of fatigue attendant on war work, 4 of pregnancy, 5 of recent moderate or large doses of sulfadiazine and 2 of striking dietary deficiency in children. It is relevant that in a family of several children the child who acquired infectious hepatitis was the one who had had chronic middle-ear disease or was recovering from one of the exanthemas. Another interesting observation was that in three homes in which only the father was sick he had been on night duty as well as daytime duty.

Character and Duration of Jaundice

The usual first sign of approaching jaundice is the appearance of bile in the urine. Thirty patients reported this symptom. The next step in most cases is a noticeable yellow tint in the scleras. The process may cease at this point, especially in children. We observed four families in which a parent had an easily recognized case of infectious hepatitis and a child, after a febrile onset, had only discoloration of the scleras for a few days. If the process is of sufficient severity, jaundice of the skin becomes evident and may last from two days to a matter of weeks, the average being two weeks. The duration of jaundice in this series is shown in Table 3. When the jaundice disappears, it goes in the inverse order, bile appearing in the urine transiently in the convalescent period. If the jaundice persists for over three weeks, some other diagnosis than infectious hepatitis must be considered. When other diagnoses

are ruled out, it is reasonable to consider that irreversible changes in the liver may be taking place¹¹⁴ and that in a few cases these will end in fatal acute yellow atrophy.

Allied Symptoms and Signs

For clarity, the allied symptoms and signs encountered in infectious hepatitis are listed in Table 4 in order of frequency of appearance. In general, the subjective complaints begin to disappear with the

TABLE 3 Duration of Jaundice

DURATION	No. of Cases
Less than 1 week	10
One week	31
Two weeks	29
Three weeks	16
Four weeks	5
More than 4 weeks	4

appearance of jaundice. This does not hold true in the severer cases. It should also be emphasized that many patients are encountered in an epidemic group who have virtually no symptoms except mild jaundice. We saw cases in family outbreaks so mild that no physician had been consulted.

Some of these symptoms and signs are interesting enough to deserve separate comment. Sore breasts and menstrual irregularities may be due to disturbances in steroid excretion by the liver as a result of hepatic-cell dysfunction.¹²⁴ Edema can probably always be demonstrated at some stage in a case of infectious hepatitis. Lucké's¹²⁵ report brought out

TABLE 4 Symptoms and Signs Other Than Those Associated with Jaundice

SYMPTOM OR SIGN	No. of Cases
Anorexia	75
Vomiting	63
Fever	62
Nausea, without vomiting	51
Symptoms of central nervous system	25
Abdominal pain	13
Diarrhea	10
Headache	7
Backache	6
Furunculosis	3
Sore breasts	3
Menstrual irregularities	3
Difficulty in reading	2
Cough	2
Urticaria	2
Ankle edema	1
"Rash"	1
Herpes labialis	1
Herpes zoster	1
Periorbital edema	1

the frequency of ascites and edema of the brain in fatal cases. Cockayne²⁷ in 1912 reported diuresis as defervescence of the disease begins. Williams¹²⁶ has commented on this in his observation on hospitalized cases of infectious hepatitis. In the 32 cases with involvement of the central nervous sys-

tem, the symptoms include irritability, apathy, drowsiness, stiff neck, temporary delirium and depression. These, with the 10 cases of headache, constitute an appreciable group of the 151 cases of infectious hepatitis. The literature reveals that other observers^{31, 129, 130} have encountered such symptoms. Lucké¹²² suggests that the loss of detoxifying power of the liver may well account for these frequently encountered symptoms. The occurrence of a rash has been previously reported,^{31, 80} as have cases of urticaria^{28, 136}. No explanation has been offered. With the well known occurrence of herpes labialis and a concomitant infection, it is surprising that only 1 case was encountered. We know of no reason why pruritus was so infrequent.

Severity

We were struck, as others^{23, 30, 70, 106, 138} have been, with the increase in severity of infectious hepatitis with age. This was not without exception, since 3 men kept at their jobs with no apparent immediate ill effect during ten days of jaundice, whereas 2 children were ill for five weeks and complained of vomiting and epigastric pain long after clinical jaundice had subsided.

Pregnant women were especially ill, as others^{50, 70, 85, 137} have noted. When one bears in mind the relation between infectious hepatitis and acute yellow atrophy and considers the fetus as an extra load for the liver, this observation is understandable. In our series there were 4 pregnant women. Two were delivered four to six weeks before the expected date. One of these women had a violent onset of infectious hepatitis, which the attending physician properly considered a toxemia of pregnancy. The diagnosis of infectious hepatitis was established on clear epidemiologic grounds. One woman aborted in the tenth week of pregnancy. One woman in her third month did not abort but had a violent and prolonged attack of infectious hepatitis, which she acquired from her daughter.

Alcohol may play a part in increasing the severity of an attack of infectious hepatitis. Damodaran and Hartfall⁸⁰ thought that this might well be the case. Observations made of protein-starved livers of famine victims in India suggest that dietary deficiency may, if severe enough, predispose to a serious attack of infectious hepatitis.¹²¹ Drugs and industrial poisons, known to be specific liver toxins, should prove important in altering the course of infectious hepatitis.

Nonicteric Cases

Liver-function tests on volunteers¹² given infectious material show that there are undoubtedly persons who demonstrate evidence of hepatic disease without developing clinically recognizable infectious hepatitis. We have included 34 such patients in this series. The onset of their disease may be identical with that of typical infectious

hepatitis. Usually bile can be demonstrated in the urine, but this occurs at times in many infections. These patients may have symptoms of gastrointestinal distress, marked anorexia and weight loss, but they never develop visible jaundice.

Physical Signs

A characteristic physical sign besides jaundice is enlargement and tenderness of the liver edge.^{28, 51, 70, 120, 125, 129} We encountered such a finding in 10 cases. The pulse is not characteristically slowed.⁵⁰ The spleen is enlarged in 5 to 40 per cent of cases.^{59, 70, 83, 138} Lucké¹²² noted enlargement of the spleen in 75 per cent of his fatal cases. Barker et al.⁸² report lymph-node enlargement, a finding that we never encountered. If the disease progresses to definite jaundice in a given case, the stools become clay-colored, as in obstructive jaundice from any cause. Edema may be present.

Laboratory Findings

Physicians caring for cases in our study used the foam test to demonstrate biliruria early in the disease. Twenty-six positive reports of biliruria were noted by them. Barker et al.⁸² have used the methylene-blue test. Albuminuria is occasionally found, perhaps simply as part of an acute febrile illness, it was encountered in 7 cases in this series. Lucké¹²² reports renal changes in fatal cases that he considers due to a cholemic nephrosis. Another report¹⁴⁰ notes cases of nephrosis in an epidemic of infectious hepatitis.

Hospitalized cases that can be carefully followed show a rise in bile pigment in the blood as the disease progresses. The level of bilirubinemia is the best index of the severity of a given case of infectious hepatitis. Liver-function tests, used in a wide variety, show changes that vary considerably.^{82, 138, 141-144} These tests are not definitely useful, since they do not parallel the clinical status of the patient. An increase in prothrombin time, especially with a poor response to vitamin K therapy, is indicative of a bad prognosis. In our series, no evidence of hemorrhagic tendency was noted. In reports of epidemics, hemorrhagic events have been noted in severe cases.^{40, 70, 80, 82, 138} Lucké¹²² reported that 109 of his 125 fatal cases showed some evidence of hemorrhage.

The white-cell count is of some value in diagnosis at the onset, when it may rise to 10,000 to 12,000. As the disease progresses, the count falls to a normal level of 8000 and occasionally to 4000. There is a relative lymphocytosis throughout the illness. Jones⁵¹ has discussed this, and Barker, Capps and Allen⁸² recently presented their findings, as have earlier observers.^{35, 58} The sedimentation time is not helpful.^{145, 146}

Differential Diagnosis

During the onset, a diagnosis is difficult, since a specific test is lacking. Acute disease of the upper

respiratory tract, grippe, influenza, an atypical pneumonia, enteric infection such as dysentery, acute appendicitis^{28, 35, 59, 117} and infectious mononucleosis come to mind. In the presence of an epidemic series of cases of infectious hepatitis, however, the problem is relatively simple. The white-cell count during onset is helpful, especially in ruling out acute appendicitis. It is elevated to levels around 20,000 in Weil's disease, which usually presents a more serious clinical picture from the start, and the specific organism *Leptospira icterohaemorrhagiae* can be found in the blood.

Infectious mononucleosis may produce jaundice.¹⁴⁷ If done at the right time, heterophile agglutination with sheep's cells will decide this point. In the tropics, malaria and sandfly fever have to be differentiated.

Sequelae

The convalescent period varies with the severity of the given case, together with the age and temperament of the patient. In young adults, we obtained uniform histories of weakness, fatigability and loss of energy as characterizing convalescence. This period ranged from two weeks to four months, with the average about one month. This time of disability was a serious problem for the armed forces both in naturally acquired infectious hepatitis⁸² and in hepatitis occurring after the giving of yellow-fever vaccine⁸ and blood transfusion.⁷

Return of the appetite was often slow. In the absence of laboratory aid, this symptom is of distinct help in estimating the return of liver function to normal. Mothers remarked of their convalescent children — and 6 adult patients agreed — that when the appetite did return it was practically impossible to give the patient enough to eat.

Weight loss was a striking feature of infectious hepatitis, as others^{82, 106} have noted. In the 47 cases in which a sufficiently reliable history was obtained, there was a weight loss of five to ten pounds in 20 cases, of ten to twenty pounds in 24 cases and of thirty pounds in 3 cases.

Relapses took place in 4 cases, with a return of jaundice in 2 of them and a prolonged period of bilirubin in 2. Returning to work too soon was the explanation in all these cases. Barker, Capps and Allen⁸² have done considerable work on this point. It is an important one for civilian physicians to consider, with diminished liver function in mind as a sequela. Altschule,¹²⁹ Kornberg¹⁴¹ and Rennie¹⁴⁴ have done careful laboratory work with patients who have recovered from infectious hepatitis and in normal controls. Their results suggest that a certain number of patients emerge from an attack of infectious hepatitis with some impairment of liver function. This work also suggests the significant fact that the impairment may not parallel the clinical course of the attack. Caravati¹⁴⁵ describes the so-called "post-hepatitis syndrome."

Prognosis

The mortality figures of different epidemics have been carefully reviewed by Lucké,¹²² who gives the range as 0.24 to 0.44 per cent. Stowman,¹⁰⁸ in his recent report of present-day infectious hepatitis, reports the death rate as ranging from 0.1 to 1.0 per cent. In the present series there was 1 death. This occurred in one of a small series of cases in an institution after three days of clinical illness, during the last twenty-four hours of which the patient was in a coma. Autopsy showed complete hepatic necrosis. Cockayne²⁷ reported such cases.

TREATMENT

General Management

Dietary management has been the standard weapon in the care of infectious hepatitis. Dible et al.¹²⁷ report histologic evidence of damage and isolation of hepatic cells from their columns in the early phase of infectious hepatitis, following which the cells can be shown to be without glycogen. Jones¹⁴⁹ considers a high sugar intake extremely important as protection for the hepatic cells. Certainly in severe cases, nausea and vomiting are dramatically relieved by intravenous dextrose in concentrations of 5 to 25 per cent. Observations made in the present series show that a high intake of sugar by mouth was the most satisfactory measure subjectively, a daily intake of 300-400 gm of carbohydrate being a reasonable goal. It is best given by mouth whenever possible.

Barker, Capps and Allen⁸² think that a high protein intake is important and quote György's¹⁵⁰ work. British workers^{151, 152} are not satisfied that high protein feeding alters the course of the disease. Handling of proteins is one of the liver's foremost and most complicated tasks, and it may be best not to give the liver large doses of protein to handle while it is disabled.

Barker, Capps and Allen remark that the matter of low fat intake is not yet settled. Experience shows that, except in the most benign cases of infectious hepatitis, the gastrointestinal tract cannot easily handle fat. Bile is being excreted with difficulty and in some cases not at all, so that fat digestion is impaired.

Vitamin K need only be added in the event of an attack of infectious hepatitis sufficiently severe to change the prothrombin level. In this series, the only evidence of unusual bleeding was a history of flooding during the menstrual flow, which was coincidental with the period of jaundice of 3 women having infectious hepatitis.

Jones¹⁴⁹ stresses the use of adequate doses of the vitamin B complex during the acute and early convalescent phases of infectious hepatitis, because the liver is temporarily unable to act in the synthesis of this vitamin. Barker, Capps and Allen,⁸² on the basis of György's experimental work, believe that too much vitamin B may be harmful.

We should like to point out that the widespread use of sulfonamide compounds at the onset of all acute infections may be injudicious in the event that the case proves to be one of infectious hepatitis. The liver acts as a detoxifying agent in handling these drugs. If, as transmission experiments with volunteer subjects suggest, the liver function is impaired before the onset of clinical symptoms,¹² use of the sulfonamides is certainly contraindicated. Perhaps these drugs can act as a precipitating factor. To illustrate this point, reference may be made to a family in which 5 of the 12 children had infectious hepatitis. The mother called one physician for 3 of the sick children and another physician for the other 2. The former were treated with a mild cathartic, a high intake of sugar and bed rest, with prompt recovery. The latter, given large doses of a sulfonamide in the onset period, had to be hospitalized and had jaundice of longer duration than did any other patients of the same age group in this series. This observation is certainly suggestive that the sulfonamide drugs should not be administered in infectious hepatitis.

Morphine and the barbiturates should be used cautiously in severe infectious hepatitis, because of the presence of active liver disease. Calomel and violent purges are only mentioned to be dismissed, as belonging to the days when infectious hepatitis was thought to be an ascending cholangitis and duodenitis, with swelling around the ampulla of Vater.¹¹⁹

Prophylactic Treatment

A new chapter in the management of infectious hepatitis is opening with the use of gamma globulin, the antibody fraction of plasma employed in the attenuation of measles. It is of no proved value therapeutically.¹²⁰ Stokes and Neefe¹²⁴ believed that they had used it successfully in the summer of 1944 to halt the progress of an epidemic of infectious hepatitis in a girls' camp. Recent reports by Gellis et al.¹²² suggest that gamma globulin confers passive immunity against infectious hepatitis for at least six to eight weeks. Prevention is desirable for pregnant women, as has been indicated. Modification will be sought as in measles because of evidence that one attack confers immunity, with few exceptions. We gave modifying doses—0.25 cc per pound of body weight—to the members of two families in Community A who were heavily exposed to infectious hepatitis by immediate family contact. Three of these subjects had episodes eight weeks later, suggesting that they were having modified infectious hepatitis. In one family in which 3 persons were given gamma globulin, a baby of nineteen months had a slight fever, was peevish, refused to eat and had light-colored stools for three days, whereas two other small children in the family, recently recovered from infectious hepatitis, were not sick at the time.

Supplies of gamma globulin will become available to Massachusetts physicians if further study confirms its usefulness in prevention and modification. American plasma has been used in controlling epidemic infectious hepatitis in the Mediterranean theater.¹¹²

SUMMARY

Infectious hepatitis occurs sporadically and in epidemic form over a wide geographical area. It seems certain that the disease is caused by a specific virus with an apparent affinity for the liver. The disease in most cases confers lifelong immunity.

The transmission of infectious hepatitis, on the basis of present knowledge, takes place by contact of a susceptible person either with a patient having the disease or with material contaminated by the causative virus. It seems certain that the virus can be carried in food. It may be carried in water.

The findings in 151 cases of infectious hepatitis in Massachusetts occurring during 1944–1945 are presented and discussed.

A plea is entered for the recognition and careful handling of infectious hepatitis. This disease clearly may cause irreversible liver changes. Our observations lead us to believe it is a serious disease in pregnant women.

Gamma globulin has no place in the treatment of the active phase of infectious hepatitis. It has been shown to be capable of producing passive immunity of six to eight weeks' duration and should be useful in the control of small outbreaks. Further study may prove that gamma globulin given during the incubation period can modify infectious hepatitis, in a manner similar to its action in measles.

An attempt has been made to include all references to epidemics of jaundice that, in the light of present knowledge, may be designated as infectious (epidemic) hepatitis. References to foreign articles, not read and not available, are included for their interest in showing the incidence and wide geographical distribution of this disease.

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MODERN GOVERNMENTAL MEDICAL PROBLEMS*

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MY brief remarks will be made from the viewpoint of one who has spent his life in the Army Medical Corps. This viewpoint, however narrow, has been broadened by the experience of two wars and the intimate association in them with mobilized civilian medicine and, between wars, a more limited association with my civilian colleagues. This country has just been through not only the biggest war in its history but also the biggest medical operation in the history of the world. I believe that everyone can profit by reviewing this experience. My comments will be limited to a review of a few crucial aspects of the Army's medical service. I shall touch on the medical problems confronting the Government as a whole and suggest one or two points of contact between the Government and civilian medical practice.

First, as to the Army, few realize that the total number of patients in all Army hospitals in 1938, both in the United States and overseas, totaled less than 10,000, which represented* during this war the patient load at a single large Army medical center. With troops in the prewar period widely dispersed and with a total of only 10,000 patients, it was clearly impossible for the Army to develop a high degree of medical specialization. We did the best we could by evacuating patients who required specialized treatment to general hospitals. This made it possible for the Army to keep some personnel at a high pitch of skill by affording them the quantity and variety of clinical material that is essential for the practice of specialized medicine.

During the war approximately 15,000,000 patients were admitted to some twelve hundred Army hospitals. For two years, between 1943 and 1945, the number of patients in hospitals was never below 270,000, and there was a peak load in April, 1945, of 544,000. At the start of the war the Army Medical Corps was slightly in excess of 1000 doctors. This number was expanded until some 47,000 were on duty. Despite the availability of these doctors, we were severely pressed for specialists and in many crucial areas simply did not have enough to go around — this in spite of the most careful supervision to see that every doctor was placed where his ability could be utilized to the fullest. As an example of this supervisory endeavor, when the hospitals in this country were busiest, a careful study by Brigadier General Fred W Rankin showed that every board member in the surgical specialties was actually practicing in his specialty or acting as a consultant in the Office of the Surgeon General or in

one of the geographical-area service commands. This scarcity of trained specialists made it necessary to organize all the general hospitals in approximately twenty specialty centers, such as those devoted to neurosurgery, ophthalmologic surgery, amputations, thoracic surgery, psychiatry, plastic surgery and tropical medicine, and to concentrate our key personnel at them. Patients requiring specialized care went to these centers, where qualified staffs were available. The success of this intricate system depended on a highly efficient medical regulating mechanism for distributing patients speedily and correctly. As many as 57,000 patients returned from overseas within a single month. Each patient was sent to the general or convalescent hospital suitable for his treatment and nearest his home.

Despite this concentration of specialists and patients, the shortages in skilled personnel were sufficiently marked to force the Army to engage in an extensive training program. Outstanding in this respect was the training of neuropsychiatrists, the Army more than doubled the numbers from civilian life. Since tropical medicine was an esoteric field, the Army had to train almost 100 per cent of the doctors used in this division. Large numbers of younger men were given training courses in anesthesia and radiology, as well as in other branches of medicine.

In this system of specialized medicine the supervision of patients and the assignment of personnel were largely the responsibility of our consultants. These men were chosen carefully and given a great amount of authority. There were consultants not only in the office of the Surgeon General but on the staffs of each major force. I regret to say that almost without exception these men who served so well during the war have now returned to civilian life. We have all realized the large contribution that they made and the benefits that were derived from their work. The high achievements and the outstanding professional advancements made during the war were dependent to a marked degree on the development and operation of this consultant system. We realize that a small postwar Army cannot possibly justify the full-time assignment of a large number of key specialists. We have, therefore, taken steps to develop a consultant system that will utilize civilian experts on a part-time basis.

You may also be interested in our plans for professional training. After the last war, our numbers were too small to permit more than a few men to continue with their studies outside Army facilities. This time we are seeking to provide adequate numbers so that a considerable part of the Medical Corps can at all times be away at school or otherwise pursuing postgraduate training. In passing, it is

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of interest that the Surgeon General has recommended and the General Staff has approved financial incentives for men who have been passed by their specialty boards

The Army's situation can be summarized in the following terms. We developed during the war a highly specialized type of medicine, which was the principal reason that we were able to furnish such excellent medical care to the sick and wounded. We are doing our utmost to perpetuate this system in peace.

Now a word concerning the medical service of the federal government as a whole. The various governmental agencies have been largely independent in thought and action, but there has always been some integration among the medical services of the Government. In prewar days the Army provided medical care for a considerable number of patients of the Veterans Administration and was also responsible for the medical care of members of the Civilian Conservation Corps.

During the war the medical services of the Army and the Navy went their own way, except in theaters of operations. There it was made evident that some integration of available means was definitely necessary. To a limited extent, Army and Navy hospitalization and evacuation operations were combined, with mutual satisfaction and effectiveness in parts of some theaters. At present, both the Army and the Navy are doing what they can to assist the Veterans Administration, which has an acute shortage of beds and personnel. For instance, the Army is holding all patients with tuberculosis who would ordinarily be discharged from the service to the Veterans Administration. We have made approximately 10,000 beds available in Army hospitals for the care of veterans.

I have studied the problem of the possibility or desirability of integrating, in whole or in part, the federal hospitals. Boston with its environs is typical of many large areas in this country. Here there are Army, Navy, Veterans Administration and Public Health Service hospitals — each operating independently. Here also there are state, county and city hospitals and large civilian teaching institutions. If we are to make the best use of our limited governmental resources, in fact of our limited national resources, it seems appropriate — at least to me — that the activities of these separate systems be somehow co-ordinated,

correlated or integrated into governmental medical centers for the care of patients entitled by law to governmental medical aid. Perhaps we should establish specialty centers, transfer patients accordingly and assign our specialists not in terms of the service to which they belong but to the hospital designated for their specialty at the same time utilizing to the full the staffs and facilities of the civilian teaching institutions. This should result in better treatment of patients. A combination of these independent facilities with their physical means and their co-ordinated staffs would provide an educational nucleus for the successful training of interns, residents, nurses and technicians for governmental service and should add to the attractiveness of a governmental medical career. As an integral part of such a medical center, there would be a central diagnostic and treatment clinic through which all except emergency patients would funnel and where the all-important outpatient treatment could be concentrated.

A significant finding in this brief study is the marked discrepancy between the available and required numbers of specialized personnel. There is no prospect whatever, so far as I can see, for the four federal agencies, operating independently, to meet their full responsibilities for hospitalization through the employment of full-time staffs. If these responsibilities are to be met, — and I am sure that each of us believes that they must be met, — the old barriers between governmental and civilian medicine must be broken down. As you know, the medical director of the Veterans Administration is seeking the assistance of medical schools and of the civilian medical profession to the greatest possible degree. The Army is looking forward to seeking the assistance of civilian consultants on a part-time basis. In short, the period of complete isolation and self-sufficiency appears to be ending.

The Army, the federal government and in fact American medicine at large face a host of serious medical problems. A preliminary review of governmental medical requirements and means indicates that we shall be hard pressed, at best, if we are to advance as rapidly as we should. Surely there is no room for the inefficiencies of isolation. The successful solution of a problem involves not only good will but intensive study. The good will of all of us exists in the attempt to solve the problems confronting governmental medicine. I believe that intensive study is needed.

ACUTE POLIOMYELITIS IN PREGNANCY*

Its Occurrence according to the Month of Pregnancy and Sex of Fetus

W LLOYD AYCOCK, M D †

BOSTON

A CLINICAL impression that poliomyelitis occurs with undue frequency during pregnancy and its possible importance in relation to susceptibility have been emphasized in previous papers¹⁻⁴. There are many reports of cases in the literature that deal with various aspects of the disease in the pregnant mother, such as effects of the disease on the mother and the fetus or obstetric problems created by the occurrence of the disease. Few reports have dealt specifically with the question of frequency of the disease in pregnancy or its significance. Within the age groups concerned pregnancy is relatively frequent and poliomyelitis is infrequent. For this reason it is difficult to establish any association between the two conditions on the basis of frequency alone. Comparisons of the percentage of cases that occur in pregnant women with the estimated percentage of women of correspond-

available on pregnancy were known to be incomplete. For one of them, the District of Columbia, the number of expected cases in pregnancy based on birth rates for the registration area — probably too high a figure for Washington — was 18. Of the 18 cases in women of twenty to forty-five years of age, 4 (22 per cent) occurred during pregnancy. In Duluth, Minnesota, there were 8 cases in adult women and 1 of these patients was pregnant, the expectancy was 0.8 per cent. Fox and Sennett⁵ report that of 6 women with poliomyelitis admitted to South View Hospital, Milwaukee, 4 were pregnant. These authors also review earlier reports such as that of Brahdy and Lenarsky, which showed that of 15 admitted women over the age of nineteen, 3 (20 per cent) were pregnant.

Waaler⁶ has recently reported that of 23 women over eighteen years of age who had poliomyelitis in

TABLE 1 *Poliomyelitis during Pregnancy in Massachusetts (1945)*

AGE	NO OF FEMALE PATIENTS	ESTIMATED PERCENTAGE PREGNANT	NO OF EXPECTED CASES IN PREGNANCY	NO OF CHECKED CASES	NO OF CORRECTED EXPECTED CASES IN PREGNANCY	NO OF OBSERVED CASES IN PREGNANCY
yr		%				
15-19	14	3.55	0.497	6	0.213	0
20-24	16	10.58	1.693	16	1.693	3
25-29	8	8.56	0.685	6	0.514	3
30-34	12	6.46	0.775	9	0.581	3
35-39	2	4.18	0.084	2	0.084	1
40-44	2	1.66	0.033	1	0.017	0
Totals	54		3.767	40	3.102	10

ing ages who are pregnant at any given time, as calculated from birth rates, have indicated an increased occurrence of the disease during pregnancy. In an outbreak in Detroit in 1939, in which the expected chance occurrence was 0.95, 4 cases were observed in pregnant women. Eleven of the paralyzed women were over the age of twenty, and in 3 of these cases (27 per cent) paralysis developed during pregnancy.⁴ This is the first study in which a record concerning pregnancy was obtained in all cases of the disease. In data obtained through the co-operation of health departments of sixty-three cities or counties in fifteen states, including Massachusetts, and in the District of Columbia, with an expected occurrence of 58 cases in 1944, 73 cases were listed. In all but two of these areas the data

1941, in an outbreak at Bergen, Norway, 7 (30 per cent) were pregnant, as compared with an estimated pregnancy rate for women in the same age group in the same locality of 6.4 per cent.

Through the co-operation of the Division of Communicable Diseases of the Massachusetts Department of Public Health, it has been ascertained that 10 of the 54 women between fifteen and forty-five years of age with poliomyelitis in 1945 were pregnant (Table 1). Actually, the question of pregnancy was verified in only 40 of these cases.

All these studies relating to the frequency of poliomyelitis concern numbers of cases too small to be convincing in themselves. In this respect the study of the question presents a problem similar to that in poliomyelitis following tonsillectomy. The relation of tonsillectomy to poliomyelitis became evident not on the basis of the actual frequency of its occurrence but from the localized occurrence of

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a particular type of the disease (bulbar poliomyelitis) at a specific interval following tonsillectomy.^{7, 8} Similar evidence of localization is seen in data collected over a period of years from various sources on cases of poliomyelitis in pregnancy.

In my records there are 236 cases in which the month of pregnancy in which the disease occurred is known, and 9 cases in which it occurred from two to twenty-three days after delivery, which is within the range of the incubation period of the disease. There is no indication of a tendency of the disease to occur at any specific period of pregnancy. There are fewer cases in the first two months of pregnancy, but this is to be interpreted as a probable dis-

and 15 women with female infants and only 4 with male infants in the third (Fig 1). There were 3 cases that occurred post partum, — five, five and twenty-three days, respectively, — suggesting that infection was initiated during pregnancy.

Confirmation of this indicated localization of poliomyelitis in the first trimester in pregnancies with a male fetus, with a shift in the last trimester to a predominance in pregnancies with a female fetus, would establish a causal relation between pregnancy and poliomyelitis. In addition, it would afford a basis for the elucidation of physiologic or endocrine factors at different stages of pregnancy, that are involved in poliomyelitis. Furthermore, such a biphasic phenomenon may be a reflection of physiologic factors in pregnancy with a male or female fetus, a conjoint study with which might afford a clearer understanding of both susceptibility to poliomyelitis and factors related to sex ratio in pregnancy.

SUMMARY

Available statistics suggest that pregnancy predisposes to acute poliomyelitis and that there is a tendency for the disease to occur in the first trimester in women who are carrying a male fetus and in the third trimester in those who are carrying a female fetus.

It is hoped that additional data relative to these matters will be made available in the near future.

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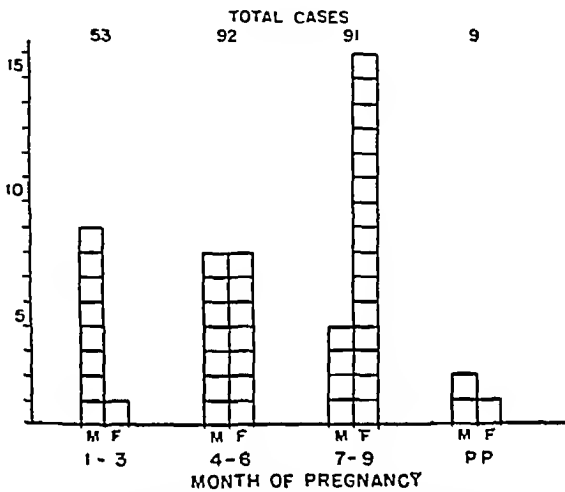


FIGURE 1 Poliomyelitis in Pregnancy according to Month of Pregnancy and Sex of Child

crepancy in the data. I myself have missed a case in early pregnancy in a nurse in a Boston hospital, whom I thought to be unmarried. Of 42 of these cases in which both the month of pregnancy when the disease occurred and the sex of the child are known, there were 8 women with male infants and 1 woman with a female infant in the first trimester, equal numbers of infants of both sexes in the second

CLINICAL NOTE

AN UNUSUAL CASE OF A FOREIGN BODY
IN THE NECK*

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THIS report, which is extremely brief, is made chiefly because it presents an extraordinary traumatic episode. There is one lesson to be drawn from it that no member of this society needs to have told him.

A few years ago, in June, a group of children were playing on the wide and high piazza surrounding their house. Suddenly a boy of six lost his balance and tumbled head foremost from the piazza into a thick mass of rosebushes. He could not get up and moaned with pain, and his head was twisted at such an unusual angle that some of the others thought that his neck was broken. He was carried into the

trating wound. When the platysma muscle was severed, the rough, jagged end of a rose stalk protruded into the wound. A firm grip was obtained on it by means of a clamp, and gentle traction was started. There was an immediate massive hemorrhage from below, apparently of venous blood. The moment this happened the stalk was jammed back, and the bleeding at once ceased. The incision was carried almost to the upper border of the clavicle. When the contents of the carotid sheath had been dissected out, the stalk was found to penetrate completely the internal jugular vein and to extend behind the common carotid artery into the thoracic cavity. The jugular vein was carefully freed and tied with No. 1 chromic catgut above and below the point of penetration of the stalk. Before further traction on the stalk was attempted, the common carotid artery was dissected out as low down as possible and a double strand of No. 2 chromic catgut was placed around it, so that it could be pulled up quickly and tied. The stalk was then pulled up gently and there was no further bleeding. The patient was given 1500 units of tetanus antitoxin.

The patient's postoperative condition was excellent, and convalescence was without any untoward event.

When the stalk (Fig. 1) was laid on the boy's chest and neck, it extended from the wound of entrance down into the right thoracic cavity until the sharp end lay just behind the 4th rib.

It may seem to take a great stretch of the imagination to see how one can draw a direct and definite analogy between a surgeon's removing a

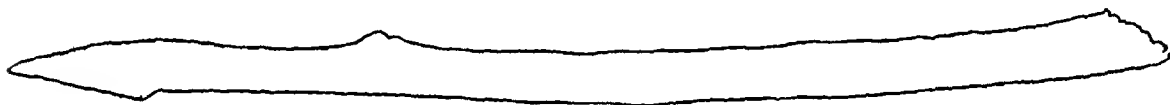


FIGURE 1 Actual Tracing of the Stalk

The total length was 19.7 cm, with an average thickness of 0.8 cm. The blunt end of the stalk, seen at the right, was palpable just behind the angle of the jaw. The sharp end of the stalk penetrated the skin behind the angle of the jaw and went cleanly through the internal jugular vein, going down inside the thoracic cavity and stopping at the level of the fourth rib anteriorly.

house, where the family physician saw him. The patient was sent to the local hospital, where I examined him. The rest of the case report follows.

Physical examination revealed a rugged boy lying on his back with his head sharply flexed to the left, a position from which it could not be moved. At the angle of the right jaw was a jagged, penetrating wound 2 cm long, and lateral to it, under the skin and platysma muscle, could be felt the upper end of a thick, rodlike foreign body, which seemed to extend a long distance downward in the neck, if not into the thorax. The rest of the examination was negative. There was no significant evidence of shock.

It was at once decided that the penetrating object was probably a long stick and that an immediate attempt should be made to remove it.

Under ether anesthesia, a short, vertical incision was made over the most prominent part of the bulge, behind the pene-

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foreign body of this sort from a child's neck and a collision at sea between two large vessels, but there is a direct one. It concerns the pushing of the rose stalk back into the neck and thorax. On September 18, 1914, the Canadian Pacific Steamship *Empress of Ireland* sank in the Saint Lawrence River with the loss of 1024 lives, having been rammed amidships by a Danish collier. The captain of the collier immediately reversed his engines and pulled his ship out, leaving the *Empress of Ireland* with a gaping hole, which made her sink almost immediately, if he had given the order "Full speed ahead," the vessels would have jammed together and the *Empress of Ireland* would probably have stayed afloat for some time.

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MEDICAL PROGRESS

DISEASES OF THE VEINS

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IN A previous review,¹ evidence by pathologists for the origin of venous thrombosis below the knees was presented. Serious illnesses, especially cardiac, injuries, operations and childbirth were proved to be the usual background for thrombosis, much of which was terminal and unnoticed clinically. The state of the blood platelets following childbirth and surgical operations was shown to predispose toward thrombosis, and patients might be more or less liable to it, as indicated by their tolerance for or sensitivity to heparin. Local conditions in the lower limbs, however, appeared to be more important factors than any others. Early ambulation did not by any means overcome such influences.

Pulmonary embolism, it was stated, was to be expected chiefly in patients over fifty years of age, but might occur in younger persons, even in those acquiring thrombosis in everyday life. It often imitated cardiac and pulmonary disease.

The distinction between an early, quiet, thrombosis (phlebothrombosis) and a late, obstructive thrombosis (thrombophlebitis) was brought out, as well as the various courses that any one lower-leg thrombosis might pursue, and the importance of this distinction was shown to lie in the necessity of applying the appropriate treatment to the different stages — vein interruptions being most appropriate for the early stage as a prevention of embolism.

Diagnosis of venous thrombosis was believed to depend not only on various local signs in the lower leg but also on an elevation of pulse rate and temperature as written on the clinical chart. Pulmonary embolism was shown to call attention to thrombosis oftener than any other single sign. The importance of electrocardiography in making the diagnosis was noted. Phlebography appeared to be regarded as a trustworthy diagnostic aid by some but not by others. Treatment of thromboembolic disease by anticoagulants and by surgical interruption of veins was discussed. The anticoagulants were gaining favor, particularly in the prevention of postoperative thrombosis, and most reports were devoted to this aspect of the subject. Little information was at hand regarding how long the treatment should be continued and how the break-off should be managed. Attempts to make the administration of heparin less expensive and more convenient than by the continuous intravenous method

were described, these including the use of a menstruum from which slow absorption could take place.

Surgical treatment appeared to have become more or less standardized, division of the femoral vein being most frequently used, but a tendency was evident to perform some higher ligations, including that of the vena cava, to cope with high, advancing processes and obscure peripheral sources of embolism. In any event, bilateral disease was always to be considered. Suction of soft thrombus from the common femoral vein appeared necessary in many cases, but it was considered not altogether satisfactory and the question of combining anticoagulants with surgery was raised.

Finally, some notes were made on the frequency with which venous thrombosis might be associated with arterial embolisms and thromboses in the limbs, a tendency that might account for some pulmonary embolism in connection with amputation for arterial deficiency.

RECENT CONTRIBUTIONS TO THE THROMBOEMBOLIC PROBLEM

Subsequent contributions to the thromboembolic problem amplify and expand previous observations, without adding anything of a revolutionary nature.

Etiology

Hunter and his associates,² continuing their earlier studies, compare a second series with their first. They undertook to determine at autopsy the incidence of thrombosis in the femoral and adductor veins of the thigh and to learn, if possible, the effect of exercise on thrombus formation. Regarding recumbency as the greatest single factor in thrombus formation, and believing that phlebothrombosis might occur within two days after recumbency had been started, they found that in patients exercised systematically until shortly before death (from any cause), only 18 per cent exhibited thrombosis at autopsy, as opposed to 53 per cent when exercise was not employed. In respect to local, mechanical factors in the legs themselves, these authors quote from Simpson's³ comment that pulmonary embolism was strikingly increased in elderly persons cared for in London bomb-proof shelters who reclined in deck chairs or something similar, the wooden crossbar causing pressure on the veins on the back of the leg and popliteal space.

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They believe that in hospitals all attendants should be embolism-conscious, particularly in respect to the lower legs as a source

Hyperprothrombinemia, as a threat of thrombosis and embolism, is further discussed by Shapiro.⁴ Observations were made on 59 cases in which present or recent thromboembolization was observed. Making use of a particular method of prothrombin estimation, Shapiro found that reactive hyperprothrombinemia could be detected by serial estimations after surgical operations, childbirth, acute coronary occlusion and some other disorders in a large proportion of cases. The detection of such a state could be used not only as an indication for treatment but also in the differential diagnosis between pulmonary infarction and other lesions presenting a similar symptomatology.

Venous pressures during various surgical operations have been studied by Davis, Gilman and Freedberg,⁵ with the thought in mind that venospasm may play a part in the observed elevated pressures found.

That such vasoconstrictions and elevated pressures may lead to postoperative venous thrombosis is suggested but of course not proved.

Clinical Course

There is an evident tendency to belittle the distinction between phlebothrombosis and thrombophlebitis, except as they represent stages of the disorder. For example, Fine and Starr⁶ encountered a soft detachable thrombus proximal to what seemed to be a typical thrombophlebitis. They declare that when embolism occurs in the presence of phlegmasia alba dolens it need not have come from the quiet, opposite leg but from the obstructed side. Thus, they recommend explorations, at an early or even an advanced stage of the acute swelling. This supports Allen, Linton and Donaldson's⁷ view that in its early progress an obstructive thrombophlebitis is a proper subject for surgery. On the other hand, Ochsner,⁸ in a complete discussion of intravenous clotting, holds the distinction between the stages to have clinical importance, not only because phlebothrombosis should be treated surgically but also because the various sorts of vascular spasm caused by thrombophlebitis, some of which may actually be contralateral, are most effectively treated by lumbar sympathetic block. Such matters will be reconsidered below under the heading "Treatment." They are mentioned here to show that the stages of the thrombosing process in the veins of the lower limbs are worthy of attention, and that if one concentrates so heavily on the embolic side of thrombosis as to ignore the distinction between the stages, one may fail to have in mind the serious reflex vascular constrictions, some of which have permanent disabling effects.

Diagnosis

Stress is laid on the value of early diagnosis, both by phlebography and physical signs. The value of the former is in controversy. Bauer¹ makes it a routine practice and pays great attention to the technic. He always cuts down on and cannulates the terminal trunk of the lesser saphenous vein below the external malleolus, declaring that its immediate deep connections, especially with the fibular (peroneal) veins, where much thrombosis originates, make it the ideal spot for the introduction of the contrast medium. Diodrast, or an equivalent iodine preparation, is used, and exposure to the x-ray from above the knee to the ankle is made with the limb in the horizontal position. This technic is believed to be decidedly more accurate than the insertion of a needle into any available superficial vein—diversion of the flow into the deep veins being forced by a rubber constriction about the upper calf—and probably accounts for Bauer's reliance on phlebography. Anderson and Patterson,¹⁰ however, make use of the needle-and-tourniquet method and depend on phlebography to determine the type of treatment to be used in cases of chronic or recurrent venous thrombosis. They regard it as unnecessary as a preliminary to ligation in cases of acute or recurrent venous thrombosis when definite local clinical signs are present. Apparently Ochsner,¹¹ who once strongly favored phlebography, now relies on it much less than formerly.

Other refinements in early diagnosis are offered by Moses,¹² who explores the posterior calf for deep tenderness by firm pressure with the fingertips and follows the discovery of a tender spot by lateral pressure between the fingers and palm, and by Tyson and Goodlet,¹³ who find that elevated venous pressure in the veins of the foot or ankle offers better evidence of thrombosis in the calf than can be secured by phlebography. Most observers look on slight enlargement, local deep tenderness and minor increases in the tone and irritability of the calf muscles, as ascertained by daily routine examinations, as most important. Spontaneous pain and pain on forced dorsiflexion of the foot are relatively late signs.

On the whole, little has been added lately to the diagnostic armamentarium, but if phlebography is to be used, the vein behind the external malleolus had better be exposed and cannulated. Consistent practice of this method in skilled hands will probably produce better results than any other one observation, the situation and extent of the process usually being revealed to the expert.

Pulmonary Embolism

The recent literature on pulmonary embolism adds a little to the understanding of both the path-

ologic physiology and the diagnosis. Attempts to study it experimentally have been made. Kinney, Haynes and Dexter¹⁴ have introduced a venous catheter into the pulmonary artery in the dog by way of the jugular vein and right heart. So far, only the method has been described, but from an informal communication, as yet unpublished, I learn that occlusion of a large pulmonary artery, by the inflation of a balloon at the tip of the catheter, produces no change in the pulse rate or respiratory rate, the systemic blood pressure, the right ventricular pressure or the electrocardiogram. Only when infarction follows do signs and symptoms appear. If, however, emboli (Lycopodium spores) are introduced into a lobe, acute symptoms, including a fall of blood pressure, dyspnea, elevated right ventricular pressure and acute electrocardiographic changes, at once occur. Apparently this reaction is due to a generalized constriction of the pulmonary arteriolar bed, that is, it is not confined to the affected lobe. Dexter and his associates are interested in the attempt to correlate these findings in human beings, and their observations should prove valuable.

Statistically, the thromboembolic problem is still being dealt with chiefly from the postoperative and post-traumatic viewpoint, although many of those most familiar with the subject evidently hesitate to rely on figures, even those secured from large clinics. Thus, Allen, Linton and Donaldson⁷ comment that venous thrombosis is commoner in certain clinics and certain geographic locations than in others and that the age of the patient is of utmost importance in the consideration of the danger of fatal embolism in thromboembolic disease. They are so impressed with the increased danger from pulmonary embolism in the aged that they have begun to employ prophylactic vein ligation in prostatic patients, cancer subjects and even some cardiac patients of the older age groups. They find little danger of fatal embolism in patients under forty years of age.

As a result of a large experience in a Swedish hospital, Bauer and Jorpes¹⁵ state that unless prophylactic and therapeutic measures are used to prevent it, thrombosis develops in 1 of every 60 patients who undergo operations or who receive other forms of treatment in surgical or medical wards, and 1 in every 5 or 6 patients who suffer thrombosis dies of pulmonary embolism. My comment is that the incidence of thrombosis given by these authors is extraordinarily low and their percentage of fatal embolisms rather high.

I consider that present-day statistics on both thrombosis and embolism merely emphasize the significance of the problem and that a study of the early signs of pulmonary embolism, together with an understanding of its nature and course, is of the greatest importance, both in medicine and in surgery.

The mode of production of pulmonary embolism has been interestingly discussed by Chapman and Linton¹⁶. Hitherto, they write, the emphasis on sudden death in the act of defecation, parturition, coition or lifting and straining at work or sports has been placed on changes in venous pressure and total hemodynamics due primarily to the heart itself. They explain so-called "bedpan" and similar deaths as due to a preliminary rise of venous pressure and blood volume in the lower limbs, by which the insecurely thrombosed veins are suddenly distended and pieces of thrombus are broken off, as pressure falls and the veins are emptied toward the heart, the embolus is washed along with the accumulated blood. Doubtless this explanation is true, but it should not be forgotten that patients suffering oppressive epigastric discomfort in the early stages of embolism may try for a bowel movement as a means of relief.

Pulmonary embolism from obscure sources is reported by Hampton, Prandoni and King¹⁷. Ten cases were observed, all of which were ambulatory and gave no history of phlebitis. The correct diagnosis was made only after considerable study. Dyspnea and chest pain were usually important clues. Probable sources of emboli were found in leg veins, pelvic veins, thrombosed hemorrhoidal veins and the plexus associated with the prostate. Anticoagulant therapy was successfully employed.

Surgical Treatment

The controversy between the advocates of ligation and of anticoagulants concerns not only the definitive treatment of thrombosis in the leg veins but also prophylaxis. I should preface the presentation of the two points of view by saying that all grant the value of maintaining muscular tone, exercising the legs and keeping up circulatory efficiency in patients forced into life in bed and by acknowledging that the advocates of early ambulation make no claim for the radical lessening of postoperative thrombosis by this means, some rather low figures (Blodgett and Beattie¹⁸) even suggesting that thrombosis is thereby increased.

The anticoagulants are represented by heparin and dicumarol and ligation mainly by bilateral ligation or section of the femoral vein, with the occasional employment of interruption of the iliac vein or vena cava.

I present first the operative surgical standpoint, which is represented most emphatically by Allen, Linton and Donaldson⁷. They believe in routine bilateral interruption of the femoral vein in the groin in all cases of thrombosis whether or not embolism has occurred, and in cases of early thrombophlebitis of the obstructive sort. Regarding the latter stage of the disease, they think that thrombectomy relieves the patient of many of the late complications that are well known to result from thrombophlebitis. They are begin-

ning to use bilateral section of the femoral vein in cardiac patients if an infarction has occurred or there are signs of thrombosis in the legs, but they have also made some prophylactic sections before any definite threat of embolism has presented itself. They have employed prophylactic ligation of the femoral vein in a small group of patients with fractures of the hip and in a good many prostatic patients. They believe that there is a definite future for prophylactic vein division, although they are not fully satisfied concerning the indications.

As regards the level of vein interruption, these authors like the idea of opening the superficial femoral vein distal to the profunda, although they make no special point of the exact level to be used. Their statistics, however, show that they have ligated the superficial femoral vein far oftener than the common vein, — in fact, in proportion of about four to one.

Fine and Starr⁶ are equally surgically minded. They are strongly in favor of bilateral ligation and prefer the common femoral level for vein interruption, believing that any resulting edema is of minor consequence compared with the greater safety of section proximal to the profunda branches. They are opposed to any distinction between early thrombosis and thrombophlebitis, for they think that embolism can occur in the presence of the latter, and they differ somewhat from Allen, Linton and Donaldson in making little distinction between the early and late stages of the obstructive, inflammatory disease. They speak favorably of ligations higher than the inguinal ligament as having less serious aftereffects than does ligation of the common femoral vein and say that such interruptions — of the common iliac vein or vena cava — seem to add no danger and result in fewer postoperative complications.

Veal and Hussey¹⁰ throw an interesting light on the level of vein interruption in a series of 84 cases, in 39 of which embolism had preceded ligation. In the latter group 9 patients suffered further embolism after ligation. Of these 9 cases, embolism was believed to have occurred from the opposite or untreated side in 5, but in the other 4 the source of the embolus was the femoral vein above the point ligated. Veal and Hussey argue from these figures that surgery failed because of inadequate surgical treatment rather than because the principle of the treatment was faulty. In the other 45 cases, in which ligation was performed before the development of pulmonary embolism, there were no cases of embolism following the operation. My own experience supports Veal and Hussey's contention. Satisfactory as is ligation below (distal to) the profunda in many early cases, unexpected tragic embolisms have occurred from a point proximal to the interruption.

There are occasional reports of other disasters following vein ligation. Dennis²⁰ operated on a fifty-nine-year-old man for a rather acute, late

thrombosis following a hernia operation. There had been considerable pain, pinkness and engorgement of the leg. The saphenous vein was thrombosed and palpable. The femoral vein was divided at the saphenofemoral junction and was found to be only incompletely obstructed. As a result of ligation of the vein, the leg at once became deeply engorged and distended with blood. Sympathetic blocks gave no relief. There was a good deal of shock, and the systolic blood pressure fell to 40. The administration of plasma brought no improvement. The leg was cold, tense and bluish-black. The deep fascia (aponeurosis) was divided from below the knee into the upper thigh on both sides of the leg, and the femoral artery was found to be pulsating normally. This operation relieved the violent, acute venous congestion, and both the leg and the patient's life were saved at the expense of considerable disability to the leg itself. My comment on this episode is that I have seen 2 cases of similar sort. In both, a large blood clot formed in the depth of the calf, both required extensive opening on the aponeurosis, and in both cases the clot became infected. Neither leg, however, was lost. Evidently, when the collateral vessels are already widely occupied by thrombus, interruption of the common femoral vein, as yet only partly obstructed, may trap an enormous amount of venous blood in the leg, resulting in both local and general circulatory damage — even shock.

Little is said by anyone about the obstinate edemas that occur following division of the common femoral vein, although Fine and Starr⁶ allude to them and Allen, Linton and Donaldson⁷ assert that they need not seriously be considered. It is my own belief that extremely careful supervision of the convalescence, with gradual resumption of exercise in the erect position, first without weight-bearing and later with it, especially if each course of exercises is balanced by a period of elevation of the legs in bed, will obviate most of the undesirable after-effects. This is especially true in the unusual and perhaps unexpected cases of serious venous obstruction following ligation of the common femoral vein.

Ochsner,⁸ whom I have already quoted as emphasizing the distinction between the various stages of thrombosis, believes in operations for phlebothrombosis, making use of lumbar sympathetic blocks for what he distinguishes as the inflammatory obstructive type causing reflex vasospasm.

De Takats and Fowler²¹ reserve ligation of the femoral vein for such patients as have suffered a pulmonary infarction and show evidence of thrombosis in the calf. For these, they recommend ligation distal to the profunda. They regard ligation of the common femoral vein as a cause of chronic edema in some cases. They are, however, greatly interested in the use of heparin and dicumarol and, as has already been stated, make a point of studying the

reaction of the coagulation time to a test dose of heparin, believing that the patient's so-called "heparin tolerance" is of real clinical importance. Their discussion of the use of anticoagulants will be considered later under that heading.

The higher vein interruptions — that is, those above the common femoral vein — are of a good deal of interest. I²² myself have advocated ligation or actual section of the common iliac vein for definitely unilateral processes — such, for instance, as occur in everyday life following minor trauma — and also for recurrent unilateral thrombosis. Interruption of the common iliac vein offers a vastly better collateral circulation than is available when the common femoral vein is ligated, especially in cases of fairly widespread thrombosis in the thigh without complete obstruction of the femoral vein itself. The difficulty with such operations is that in many chronic or recurrent processes both common iliac veins may be very friable and easily injured, that the left, for anatomical reasons, is often inaccessible and that a general anesthetic is required, as opposed to the local infiltration so satisfactory in the case of the femoral vein. It will be noted, however, that Fine and Starr⁶ regard these operations as adding no appreciable risk. Bancroft²³ reports a satisfactory experience with them in a study of 12 cases in which sixteen thrombectomies were performed for thrombosis discovered at the operative level, but notes 1 death from embolism. All his operations were iliac explorations, and three were bilateral. He gave heparin by Loewe's method (see below) following operation and regards high vein sections as being on the whole safe and life-saving. Satisfactory as many operations on the common iliac vein have proved to be, they do not cover the problem of bilateral thrombosis, since separate incisions are required for the two sides and this seems a decidedly overcomplicated procedure when ligation of the vena cava can be performed at one stroke at only a little higher level.

Divisions of the vena cava have been employed in many cases when a bilateral process is present and appears to be uncontrollable or when the source of serious embolism is so obscure that one authoritative step to stop it must be taken. O'Neil²⁴ has had a highly satisfactory experience with these operations, regards them as exceedingly useful, has run into little danger in performing them and finds little disability afterward. He reports a considerable series of cases. A favorable account of ligation of the vena cava, with a history of the procedure, is offered by Northway and Buxton.²⁵ Still another report comes from Gaston and Folsom,²⁶ and Kern and Berman²⁷ record a successful division of the vena cava for a septic thrombosing process. It is unnecessary to emphasize that the approach to the vena cava offers difficulties not inherent in operations at a lower level. It is easy to reach the great vein through a lateral retroperitoneal incision, but the field offered by the unilateral exposure is so limited that if some of the delicate

lateral veins entering the vena cava are torn, as by even the gentle pressure of a blunt ligature-carrier, it is extremely difficult to control the bleeding. Linton, in a personal communication, states that the best approach is by a right paramedial incision of considerable extent, pushing the peritoneum and the abdominal contents toward the left and obtaining a direct view of the vena cava and its branches from in front. Others have approached the vena cava transperitoneally. One must also realize that in some cases so enormous an amount of blood is trapped in the lower half of the body by sudden interruption of the vena cava that patients are occasionally thrown into serious or even fatal shock unless elevation of the legs is immediately and persistently employed.

Altogether, the operation has many times appeared to be life-saving but should not be undertaken by those not familiar with the difficulties of handling large blood vessels under a variety of circumstances.

This concludes the case for the surgical interruption of veins in the control of thrombosis and embolism. That for the anticoagulants is now to be presented. Special considerations, as in the case of fractures, will be taken up separately.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 32311

PRESENTATION OF CASE

A fifty-three-year-old man entered the hospital with jaundice

For several years the patient had had slight postprandial gaseous indigestion produced by fatty foods, this was seldom troublesome, since he had been on a low-fat, low-protein diet because of gout of thirteen years' duration. He had taken colchicine during exacerbations of the disease, with great relief. One and a half years before admission he had the first attack of a colicky right-upper-quadrant pain, after which there was no further difficulty until six months before admission, when he had several episodes of similar pain. At that time a cholecystectomy was performed at another hospital. The gall bladder contained numerous stones. The common duct could not be identified. Postoperatively the patient became jaundiced and began draining large quantities of bile through a laterally placed stab wound. Six weeks later he was re-explored by another surgeon. Again the common duct could not be found. The portal vein was accidentally opened, and the patient lost a great deal of blood. Postoperatively bile drained through the wound, and the previous sinus closed. The jaundice disappeared. Subsequent to the first operation the stools had been acholic, but they turned brown after the second operation. Bile continued to drain until six weeks before admission, when the second sinus closed. Three weeks later the skin became mildly jaundiced and began to itch. Four days before admission there was pain in the right upper quadrant and in both shoulders. This was not related to respiration. During the following three days the patient vomited everything taken by mouth. He continued to have pain and passed scanty, dark urine. The stools were small and slate gray.

Physical examination showed moderate jaundice and slight diffuse tenderness in the right and left upper quadrants. The site of the previous sinus was extremely tender. There were diminished breath sounds and crackling inspiratory and expiratory rales at both lung bases.

The temperature was 97°F, the pulse 100, and the respirations 24. The blood pressure was 100 systolic, 60 diastolic.

The white-cell count was 22,300. The urine was dark amber and gave a + reaction for bile. X-ray films revealed linear bands of density at both lung bases. The upper lung fields were clear. The diaphragm was high on both sides. A film of the abdomen showed the common and hepatic bile ducts to be filled with gas (Fig 1), no dilated loops of bowel were seen.

One hour after admission the patient began to have severe, agonizing left-upper-quadrant pain and quickly developed marked tenderness and spasm of the entire upper abdomen, particularly in the left upper quadrant. Peristalsis was high pitched and hyperactive, alternating with long periods of silence. He was writhing with pain when examined.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR FIORINDO A SIMEONE I think it might be interesting to see the x-ray films first.

DR JAMES R LINGLEY This is a film of the chest showing the high diaphragm on both sides, with linear bands of density at the bases consistent with atelectasis. This plain film of the abdomen shows a moderate quantity of gas in what looks like the colon, which does not appear to be appreciably dilated. This is the gas bubble of the stomach, and in the right upper quadrant it can be seen that the common bile duct, the hepatic duct and the radicles are completely filled with gas. There is no definite mass, and no evidence of stone.

DR SIMEONE I should like to discuss this case from the point of view of complications following the removal of a gall bladder for stones. The patient had postprandial gaseous indigestion produced by fatty foods, and a diagnosis of cholelithiasis was made, for which an operation was performed. He had gout of some twelve years' duration and took colchicine. I thought of the possible lesions associated with gout, but could not find any to account for the symptomatology before or after operation, nor could I find anything that suggested a toxic reaction to the occasional taking of colchicine during a few exacerbations of gout. The gout and colchicine may therefore be considered as purely incidental.

A year and a half before admission the patient had the first attack of colicky pain in the right upper quadrant, so that if this was gallstone colic he had his first attack at the age of fifty-one, which is perhaps slightly unusual but not too much so. Following that one attack he had no more trouble. If he had stones they were silent until six months before admission, when he had several episodes of similar colicky pain in the right upper quadrant, which probably appeared at frequent intervals, suggesting a stone in the common duct, although there is nothing in the record about nausea, vomiting, jaundice or chills and fever. Cholecystectomy was performed at another hospital, and the gall bladder was described as containing numerous stones. It

would be helpful if one knew, in addition to the number of stones, how large they were. Although at operation the common duct could not be found, presumably it was looked for, as indicated by the note that the common duct was not found. I am left with the impression that the stones were smaller than the caliber of the cystic duct, which led the surgeon to look for the common duct.

Postoperatively the patient became jaundiced and began draining large quantities of bile through a laterally placed stab wound. This, of course, brings up a problem that is generally feared in gall-

anomalous and therefore difficult to recognize, or was located in densely scarred gastrohepatic omentum and difficult to dissect and identify. At the second operation the portal vein was accidentally opened, and the patient lost a great deal of blood. We are not told what happened at the second operation, but I imagine that little more was done after the puncture of the portal vein. I suspect that the accident occurred early in the operation, probably before the surgeon had a chance to mobilize the duodenum to identify the common duct transduodenally, this procedure might have favored the

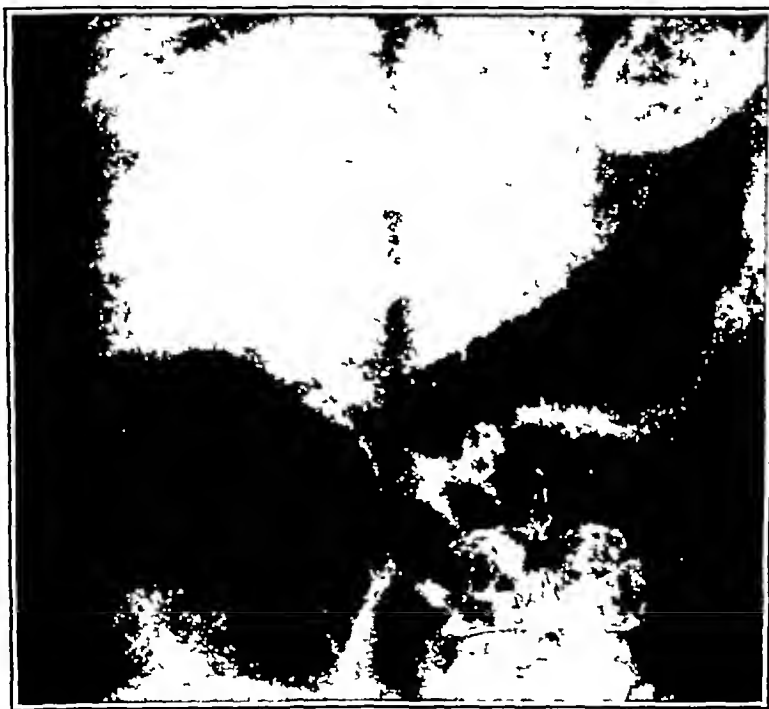


FIGURE 1 *Roentgenogram of Abdomen*

bladder surgery, namely, injury to the common duct. In removal of the gall bladder the common duct is sometimes injured through outright carelessness, less often it is injured because of one of several anatomic anomalies of which the surgeon is not aware until too late. Although this is the first accident to suspect in this case, two points in the subsequent history make me doubt such a diagnosis. In the first place, the roentgenogram showed a common duct filled with air. Secondly, jaundice disappeared and bile appeared in the stools, suggesting that the common duct re-established continuity with the duodenum or other part of the bowel spontaneously after the second operation, which was done because of the jaundice and because of the persistent bile-draining sinus six weeks after the first operation. Again, the common duct could not be found. Perhaps the stricture had been resected or was

establishment of a fistula between the bile ducts and duodenum. It is difficult to understand how the surgeon opened the portal vein without encountering the common duct, because of the anatomic relations of the two structures.

Postoperatively bile drained through the wound, the persistent sinus eventually closed, and the jaundice apparently disappeared, because a new external fistula was formed from the common duct, or perhaps the old fistula was cut across and drained through the wound. The stools turned brown after the second operation, however, so that bile must have been getting into the intestines. I should like to explain that on the basis that at the time of the first cholecystectomy the patient probably had a stone in the common duct as well, which did not cause jaundice until after the operation and somehow became dislodged temporarily after the second

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tried to repair the duct, but in attempting to make the exposure the portal vein was entered and the operation had to be terminated after a stormy time on the operating table. The patient gradually recovered, and was finally slated to come to this hospital for repair at an optimum time. The surgeon called, however, and said that if the patient did not get into the hospital within three or four days, he would be dead at home. Consequently, he entered the hospital as an emergency case and was rather ill when first examined. A few hours after entry, having been previously quite comfortable, he began to have severe, agonizing, colicky abdominal pain, with high-pitched peristalsis. An x-ray plate was made, and the report that we received was that there was gas in the liver radicles and also dilated loops of small and large bowel. The radiologist in charge that night thought that this represented intestinal obstruction. The gas in the biliary tract, we thought, probably entered from a spontaneous fistula into the duodenum, although the possibility of a transverse-colon fistula had to be considered. Since the pain was colicky and because of the dilated loops of bowel and the fact that the abdomen quickly became tender throughout, we thought it most probable that he had developed a strangulating obstruction, although as a second possibility imminent perforation of an abscess through the liver into the peritoneal cavity near the common duct was considered.

A right-upper-quadrant incision was made. No evidence of intestinal obstruction could be demonstrated. On coming down to the region of the foramen of Winslow we found pus that had a foul odor, indicating that an abscess was perforating at this point. We assumed that it was coming from the liver or from the common duct. We were able to open into the hepatic bed and, finding the stump of the common duct, to insert a T tube into the common duct and into the viscus that was adherent at the portal fissure. The patient's condition was poor at operation. He drained bile for twenty-four hours freely through the tube. The bile was followed by pus and then by fecal drainage. He never really improved, and died almost on the same schedule as his doctor had predicted.

CLINICAL DIAGNOSES

Small-bowel obstruction
Cholechojejunal fistula
Obstructive jaundice
Pulmonary atelectasis

DR SIMEONE'S DIAGNOSES

Residual stone in common duct
Acute pancreatitis

ANATOMICAL DIAGNOSES

Benign stricture of common bile duct
Cholechooduodenocolic fistula

Multiple abscesses, hepatic, subhepatic and diaphragmatic

Acute fibrinopurulent pericarditis

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY Autopsy showed a complicated picture. There was a double fistula from the remnants of the common duct, one went into the duodenum, and the other into the hepatic flexure of the colon. There were two benign strictures in the common duct, one above and one below the area of the fistulas. There was also a communication into a hole in the liver, which was probably an abscess cavity, and led to the left hepatic duct. A small old abscess was found in the region of the head of the gall bladder. There were dilatation of all the intrahepatic bile radicles, multiple abscesses throughout the liver and a considerable subhepatic abscess. Infection had extended into the diaphragm, which was split into two leaves by a collection of pus. There was also acute fibrinopurulent pericarditis. We could not find persisting stones anywhere, and the pancreas — surprisingly enough, in the face of all this biliary infection — showed no trace of inflammation.

DR BENEDICT I do not see how the agonizing left-upper-quadrant pain is explained.

DR WELCH I thought that was explained at the time of the autopsy, because in dissecting between the leaves of the diaphragm we found this great abscess, which must have contained 500 cc of pus. The pus was entirely above the peritoneum and was not in the pleura. It finally perforated into the pericardium.

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CASE 32512

PRESENTATION OF CASE

A fifty-nine-year-old housewife entered the hospital complaining of pain in the epigastrium.

Five years before admission the patient, who had previously had fair digestion and no abdominal pain, suffered a severe hematemesis. Thereafter there was almost continuous epigastric discomfort. When she worked too hard or stretched, pain developed in the upper abdomen. There was no further vomiting or passage of black stools after the original episode. One month before admission a severe mid-epigastric pain doubled the patient and required morphine for relief. It radiated slightly to both sides. From then on she had continuous nagging pain, without other symptoms. During this period

operation. Stones in the common duct are not an unusual finding in cholelithiasis. In 1940 Allen and Wallace¹ reported that in a series of 860 cases in this hospital during a four-year period roughly 1 out of 5 patients with cholelithiasis had stones in the common duct and that in almost half (46.8 per cent) the cases in which the common duct was explored, stones were found. It is therefore not unlikely that this patient with numerous stones in the gall bladder had a stone in the common duct, which was not found at the first operation.

Bile continued to drain until six weeks before he was admitted to this hospital, where the second sinus closed. Three weeks before admission the skin became mildly jaundiced and itched. For three weeks, then, the patient had no external biliary fistula and no jaundice. Four days before admission there was pain in the right upper quadrant and in both shoulders. This was not related to respiration. For the next three days the patient vomited everything that he took by mouth. That could have been due to recurrent common-duct obstruction from stone or a leak through the old biliary sinus, and a subhepatic abscess, with pressure on the duodenum, might have formed. He continued to have pain and passed brown stools. Apparently bile was still reaching the intestine.

The diminished breath sounds and crackling inspiratory rales are accounted for by the elevated diaphragm, which resulted from inflammation beneath it and which caused atelectasis in both lower lobes. Physical examination showed diffuse tenderness in the right and left upper quadrants, suggesting an inflammatory lesion in the upper abdomen, but the temperature was recorded as 97°F, so that unless this man was in extremis as a result of the infection, he was not showing the expected temperature rise, which may be taken as evidence against a subhepatic abscess. The pulse was rapid, and the blood pressure low. These findings, along with the low temperature, suggest several possibilities. Perforation of a malignant or benign lesion of the stomach is unlikely. The roentgenogram of the abdomen did not suggest mechanical intestinal obstruction, which should be considered because special mention is made of intermittent high-pitched peristalsis. The history is consistent with mesenteric thrombosis, but again there was no x-ray evidence of intestinal obstruction. The temperature, white-cell count and blood pressure are consistent with mesenteric thrombosis or with acute pancreatitis. The history of repeated abdominal operations, with some inevitable infection, favors the former, the jaundice and cholelithiasis and the suspicion of choledocholithiasis favor the latter.

If the presence of an intact common duct is accepted, the x-ray finding of gas in the biliary tree is difficult to explain. The most plausible explanation for such gas is a fistula between the bile ducts and the duodenum. No evidence of injury to the du-

odenum, which might have favored the establishment of such a communication, was found, and no mention is made of digestion of the skin about the draining sinuses. In rare cases, gas regurgitates into the biliary tree through the papilla of Vater.² In one case these ducts filled with barium during an examination of the stomach for carcinoma, which made me think that the final episode was a perforation of a cancer of the stomach, but there is nothing in the history to indicate such a diagnosis. Cases have been encountered with regurgitation of air and injected barium through the papilla of Vater when a stone has been impacted in the papilla.² I should like to explain the course of events in this patient on that basis. The acute episode of severe agonizing left-upper-quadrant pain could have been due to acute pancreatitis secondary to stone in the ampulla. My final diagnosis is therefore residual stone in the common duct, with acute pancreatitis.

DR EDWARD B. BENEDICT: How about a stone in the pancreatic duct?

DR SIMEONE: I do not believe that that would produce jaundice unless it were close to the junction with the common duct.

DR BENEDICT: I mean in addition to the pancreatitis. Such stones are often demonstrated by x-ray.

DR TRACY B. MALLORY: Does one ever have pain with stone in the pancreatic duct? There is no muscle in the duct, and I do not see how it could go into spasm.

DR SIMEONE: Cases with calcification have been reported in the head and body of the pancreas, with excruciating pain, which is relieved by subtotal pancreatectomy.

DR MALLORY: Pancreatitis would offer a good explanation of the pain, but I doubt that colic can arise from the pancreatic duct.

DR LINGLEY: I do not believe that we have seen gas in the common duct with cancer of the ampulla. Is it not rare?

DR SIMEONE: I think that 5 or 6 cases are reported in the literature with gas in the biliary tree in the presence of an intact common duct and papilla of Vater.

DR LINGLEY: Unfortunately, the cases that we have seen have been due to fistula between the duct and the bowel.

DR CLAUDE E. WELCH: A number of considerations that Dr Simeone has not mentioned troubled me. If I can interpolate a few facts into the history, this may be made clearer. In the first place, there was no question in the mind of the doctor who referred the patient to us that his patient had had an injury of the common duct. Ever since Dr Allen³ published his method for the surgical repair of injuries of the duct, we have been confronted with many of these cases. In the case under discussion, at the time of the second operation, the surgeon

Hodgkin's disease, lymphoblastoma and lymphosarcoma may cause infiltration, with subsequent ulceration of the stomach wall, and it is frequently quite impossible to do more than suspect that a given lesion may be on this basis. But characteristically the picture is that of a rather plastic stomach wall, with overlying, thick and rigid mucosal folds within which the ulceration may be present. Such a lesion does not seem likely.

Areas of ulceration infrequently occurring in gastritis are usually small and multiple, and the findings of gastritis predominant.

Among the granulomas of the stomach in which ulceration occurs, syphilis is most frequently thought of and only rarely seen, as in ulceration in the thickened, stiff and shrunken stomach wall of a so-called "leather-bottle stomach." Ulceration of a gummatous lesion in the stomach is still rarer — enough to be thought of only when nothing else seems to fit the diagnosis and when the serologic findings are indicative. More rarely still has ulceration in the stomach, said to be on an acid-fast basis, been described in a patient with pulmonary tuberculosis. In the case under discussion the serologic findings were apparently not incriminating, and the chest was certainly not.

Neoplasms arising outside the stomach that have become adherent to it occasionally cause ulceration of the mucosa, most frequently, perhaps, cancer of the colon, but nothing in this case suggests anything amiss in the colon. Tumors of the pancreas or other abdominal tumors, such as lymphoma, also cause ulceration. The gastric diverticulum that are occasionally seen in the fundus of the stomach should not be mistaken for significant lesions.

This leaves to be considered the two most frequent causes of ulceration of the gastric mucosa: benign ulceration of the stomach and an ulcer due to a cancer of the stomach. The old problem concerning the relation of cancer to pre-existing ulcer will not be discussed. I should like to mention what I think is the real burden of this presentation. I do not want to be an apologist, but it seems well to point out the limitation of the roentgenologist in determining in every case whether or not an ulcer is benign. The limitations are much the same as those imposed on the surgeon when he has the abdomen open and the viscus exposed and on the pathologist when he has only the gross specimen, with the added drawback of his inability to observe small metastases to the liver and regional lymph nodes. Usually the differentiation is quite reliable. There are findings that suggest a malignant lesion, and others that are either equivocal or difficult to assay. As a rule it is easier to say that a lesion is malignant than that it is not. Demonstration of malignant changes have often to await detailed histologic study.

Characteristically a benign ulcer lies on or close to the lesser curvature, but many ulcers in this position have proved to be malignant and others located elsewhere in positions often thought to be unusual for benign ulcers have proved to be non-malignant. The last three simple ulcers on the greater curvature seen in this hospital were benign. The high incidence of malignant changes in peptic ulcers is well known. The size of an ulcer is not a reliable criterion, neither is roughness or smoothness of the base. Irregularity may be due to tumor granulations or food particles. The duration of the disease is also not diagnostic. The course of an ulcer under active management may be helpful: if it heals and leaves no rigidity of the wall, it is quite likely to be benign, but an ulceration in a tumor that heals or fills with tumor or food usually leaves stiffening behind, which represents tumor infiltration. Perhaps the most reliable sign denoting ulceration in a tumor is the actual demonstration of the tumor in which the ulcer lies. A benign ulcer lies or projects beyond the wall of the stomach — the other lies within the projected wall of the stomach intraluminally, giving rise to the so-called "meniscus sign of Carmen." This is not infallible, however. A large inflammatory reactive mass may be mistaken for tumor, or an ulcer in a tumor may penetrate deeply, and the finding is not always easy to demonstrate with complete satisfaction.

Rigidity of the stomach wall about an ulcer such as that in the case under discussion is most frequently, but not always, due to infiltration by tumor, as is also gross deformity of the gastric mucosal folds about an ulcer.

In this case one would like to speculate on the likelihood of a gastric ulcer, atypical in location and for this reason long overlooked, that had recently perforated — possibly into the liver, which lies in contact with this part of the stomach. This could have resulted in the formation of a large inflammatory mass, which was the palpable tumor and which might have been mistaken for the mass about the visualized ulcer. The location was unusual, however, and the ulcer was large, and rigidity of the wall was described. And there was a mass that presented a shelf-like defect — an intraluminal tumor in which the ulcer was situated. And since no subsequent examination demonstrated this to be a faulty observation, it must be accepted.

The diagnosis of leiomyosarcoma still intrigues me, in spite of the fact that the x-ray findings are not typical. The story is not inconsistent with cancer of the stomach, which is by far the most frequent tumor. The x-ray findings gave evidence of some kind of tumor. This all leads to a diagnosis — admittedly based largely on a single examination — of ulceration in a cancer of the fundus. The safest thing, of course, would be to say an ulcerating lesion of the stomach that was not conclusively benign.

the patient had been on a Sippy regime. There was a recent weight loss of 9 pounds from her normal weight of 107 pounds. Numerous x-ray films were taken during her illness, including a gastrointestinal series six months and a chest film two weeks before admission, which were said to be negative. Because it was thought to emanate from the spine the pain was treated by a back brace. She had had slight low-back pain, attributed to rheumatic changes shown in x-ray films of the spine. There had been no jaundice or acholic stools, constipation, diarrhea or distention.

The past history was not remarkable, except for the implantation of radium per vagina for menorrhagia at the menopause, thirteen years before admission.

On physical examination there was a firm, non-tender mass in the epigastrium, which moved with respiration and transmitted a powerful aortic pulse. Both kidneys were palpable.

The temperature was 98.0°F, the pulse 70, and the respirations 18. The blood pressure was 160 systolic, 90 diastolic.

The hemoglobin was 10.2 gm per 100 cc of blood. The white-cell count was 10,600. The urine was normal. The stool was light brown and gave a negative guaiac reaction. X-ray studies revealed a crater, 3.0 by 2.5 by 2.0 cm, in the posterior wall and lesser curvature of the stomach just below the cardia. It appeared to be in a filling defect, the upper margin of which was somewhat shelf-like. The remainder of the stomach showed rather small peristaltic waves, without definite evidence of rigidity except for an area about 3.0 cm below the lower margin of the lesion. The duodenum and the rest of the intestine were normal. One hundred cubic centimeters of fluid aspirated from the fasting stomach contained 3 units of free hydrochloric acid per cubic centimeter; there was no free hydrochloric acid in the 8-cc specimen after alcohol. An electrocardiogram was normal.

A gastroscopy was done on the tenth day. The instrument was blocked at the cardiac orifice, but it was possible to see beyond the obstruction to the lesser curve, where a 3-cm ulcer was visible on the anterior wall. It had slightly irregular margins and a sloughed base.

Operation was performed on the twenty-sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR MILFORD D SCHULZ. This is the story of a patient presenting a complaint of abdominal discomfort and pain of which she had not been entirely free for five years. The first episode was accompanied by hematemesis, which was not repeated. She had received treatment intended to control a peptic ulcer, although there had never been visible evidence of a gastric or duodenal lesion until after the acute episode a month before ad-

mission, when further study of the upper gastrointestinal tract with the help of a roentgenologist and an endoscopist demonstrated a large ulcerating lesion high on the stomach wall. The variance of opinion regarding whether the lesion was on the anterior or posterior wall is understandable when one considers the problems of orientation in this area.

This problem resolves itself into the differential consideration of ulcerating lesions of the stomach.

Since I should like to discuss this case mainly from the standpoint of a roentgenologist, a review of the x-ray findings might be helpful. The ulcer, which was 3 cm in size, was unusually high and although not on — but toward — the lesser curvature, it seemed in fact to be above the lesser curvature and in the fundus. The ulcer did not appear to protrude beyond the stomach entirely but rather to lie intraluminally as though in a mass about which a so-called "shelf" was described. This was probably the fluoroscopist's observation and is most important. It is certainly not an observation, however, that cannot be wrong, for the fundus is sometimes difficult to examine satisfactorily. No abnormality of peristalsis was demonstrated, although some rigidity was described just below the crater. Again, when the lesion is beyond the reach of the palpating hand, this observation is uncertain. The mucosal pattern did not seem to be altered, except in the immediate vicinity of the crater, where the appearance of convergence of folds toward the ulcer may have been merely apparent, owing to the projection of the fundus. No soft-tissue mass outside the projected wall of the stomach was demonstrated.

Tumors of the spindle-cell variety may be benign or malignant, are slowly growing and often ulcerate, sometimes quite early, leading to abrupt and intermittent bleeding, which may be the only presenting complaint. The history in this case is not incompatible with such an occurrence. But these tumors lie in the wall of the stomach and grow submucosally, more or less equally in all directions, stretching and bulging the stomach wall into a smooth crescentic defect over which the folds of an intact mucosa are smoothed out except where the usually somewhat centrally placed ulcer extends into the large, rounded soft-tissue mass outside the wall of the stomach, which can occasionally be seen on adequate x-ray films. A spindle-cell tumor is suggested by the long history, with early and non-continuous bleeding, by the palpable mass, and by the recent episode after which a previously undiscovered ulcer was found, which may have meant recent ulceration, furthermore, an un ulcerated extramucosal spindle-cell tumor in this position can easily be overlooked. Since none of the characteristic x-ray findings were present in this case, I shall dismiss this diagnosis. It might still be entertained, however, as an outside chance.

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HOSPITAL CARE OF VETERANS

ELSEWHERE in this issue of the *Journal* there appears a report from the secretary of the Deans' Committee of Harvard, Boston University, and Tufts College medical schools concerning the status of the Veterans Administration Hospital in West Roxbury. Representatives of these three schools have undertaken to provide the resident, attending and consulting staffs of this institution with the view of making it into a hospital that will be recognized as acceptable for resident training not only by the American Medical Association but also by the various specialty boards. In addition, it is anticipated that the same procedure will follow when the 2000-bed Cushing General Hospital in

Frammingham is turned over to the Veterans Administration

All this is in accordance with plans laid down by General Omar Bradley and by Dr Paul R. Hawley, former chief surgeon for the European Theater of Operations and now chief medical director of the Veterans Administration. The project is a great step forward, primarily, of course, it guarantees better care of the veteran, but it also provides a method of giving further hospital training to the large number of young doctors in the armed services who had a much-shortened period of medical-school and intern education. The affiliation of the Veterans Administration hospitals with medical schools is coming into effect throughout the country, and the impression has already been gained that an increased turn-over of patients has resulted—in other words, the average length of time required to treat veterans has been reduced because of the improved situation regarding medical service and personnel.

There can be no doubt that this plan, energetically pursued, will result in great benefit to veterans, to recently graduated physicians and, because of reduced costs resulting from better medical care, to the public at large. There is much work yet to be done, but certainly if the profession co-operates wholeheartedly and sympathetically, this forward step in caring for the enormous and unavoidable by-product of war will result in improvement in the handling of one of the major medical and sociologic problems of the country.

"IN THY MOST NEED"

THE Institute of Pastoral Care, established at the Massachusetts General Hospital in 1944, had its beginnings in an address delivered by Dr Richard C. Cabot over twenty years ago entitled "A Plea for a Clinical Year for Theological Students." Out of this plea came the establishment of a training course at the Worcester State Hospital in 1924 and, in the belief that a broader experience could be gained from a general hospital, the beginning of a continuing program at the Massachusetts General Hospital in 1933.

DR EDWARD B BENEDICT The gastroscope met with complete obstruction at the cardiac orifice. That usually means a carcinoma, but in a case of ulcer high up close to the cardia with spasm, the gastroscope may meet with complete obstruction. The ulcer itself looked irregular, in spite of a smooth margin. That observation has been slightly in favor of cancer, although severe gastritis around an ulcer may produce a similar effect. I thought from the gastroscopic standpoint that the ulcer was probably malignant, although the five-year history seemed rather long. It seems to me in any of these cases that the important thing to decide is not whether or not the lesion is benign but whether or not to operate. I should rather operate on a benign ulcer erroneously than to let a malignant ulcer go without operation. The decision was therefore made to operate on this patient.

CLINICAL DIAGNOSIS

Carcinoma of stomach?
Gastric ulcer?

DR SCHULZ'S DIAGNOSIS

Ulcer in cancer of stomach

ANATOMICAL DIAGNOSIS

Benign peptic ulcer

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY This patient was operated on by Dr Richard H Sweet via the trans-thoracic route, which is obviously indicated with a lesion as high in the cardia as this one was. He found a very indurated mass in the stomach, which was densely adherent to the pancreas. He carefully searched the abdominal cavity but found no evidence of metastases. He was still uncertain whether the lesion was benign or malignant, but believed that it was readily resectable and proceeded with the operation. The only difficulty met with was in dissecting it free from the pancreas. The microscopic sections showed a benign peptic ulcer, with no evidence of neoplasm.

The unusual points in the case have been brought out by Dr Schulz: this lesion was much higher in the stomach than benign ulcers are usually found, and the area of ulceration was considerably larger than that ordinarily seen with benign ulcers. There is essentially no limit to which a benign ulcer can reach, however. I have seen one 10 cm in diameter, three times as large as the one in the case under discussion.

ishment *Provided*, that such person is supplied with a written statement from the patient's physician or, in the case of an establishment engaged in the care and treatment of the sick, from a responsible official thereof who is a practicing physician, and such written statement shall be valid for a period of not to exceed sixty days from the date of issuance and shall specify (i) The milk fat content of cream required for such use, (ii) the daily quantity of such cream, and (iii) with regard to the necessity of such cream for supervised medical treatment *Provided further*, that such written statement shall not be valid for obtaining such cream unless approved by a public health officer who is a physician, or by the secretary of the county medical society of the county wherein such patient resides or such establishment is located

2 Upon application by one or more persons in any area or region and after demonstration to the satisfaction of the Administrator that compliance with the provisions of (b) (1) hereof will not tend to conserve milk fat for defense and essential civilian needs, or upon the initiative of the Administrator, the Administrator may grant an exemption from the provisions of (b) (1) hereof to any or all persons in such area or region specified by the Administrator

Finally, any person who feels aggrieved by this regulation may file a petition for relief with the War Food Order Administration and send his or her communication to the War Food Order, No 149, Dairy Branch, Production and Marketing Administration, United States Department of Agriculture, Washington 25, D C

MICHAEL A TIGHE, M D, *Secretary*

DEATHS

CHANDLER — Harold B Chandler, M D, of West Newton, died July 14 He was in his sixty-first year

Dr Chandler received his degree from Harvard Medical School in 1911 and had limited his practice to ophthalmology His widow, two daughters and a son survive

ELMS — Evelyn B Elms, M D, of Waban, died July 14 She was in her fortieth year

Dr Elms received her degree from Tufts College Medical School in 1932 She served as a lieutenant in the Navy Medical Corps during World War II and was a fellow of the American Medical Association

Her mother and a brother survive

CORRESPONDENCE

RESIDENCY TRAINING IN MASSACHUSETTS VETERANS ADMINISTRATION HOSPITALS

To the Editor The establishment of a Department of Medicine and Surgery in the Veterans Administration, as provided for under Public Law 293, has led to the development of an extensive residency training program in many Veterans Administration hospitals It is hoped that this program will result in securing for the veteran patient a standard of medical and surgical care comparable with that rendered in the best civilian hospitals To secure the best advice and assistance in carrying out such a program, the Veterans Administration has called on the deans of schools of medicine to give counsel in all matters pertaining to the education and training of residents and is, with the help and advice of the deans, appointing qualified staffs of part-time civilian specialists These specialists will carry on much of the residency training

The Deans' Committee for the Massachusetts Veterans Hospitals consists of Dean Dwight O'Hara of Tufts College Medical School, chairman, Dean C Sidney Burwell of Harvard Medical School, Dean Donald G Anderson of Boston University School of Medicine and Dr Dale Friend, of Harvard Medical School, secretary Each dean has selected two advisors, one in medicine and one in surgery These

advisors are Drs Laurence B Ellis, James M Faulkner, Roger C Graves, Chester S Keefer, Reginald H Smithwick and Augustus Thorndike

Part-time civilian specialists are divided into two categories depending on the degree of experience and skill, teaching qualifications and need The first group consists of senior physicians of outstanding ability — those of professional caliber in the medical schools or of equivalent standing among the practicing profession of the community These men are called consultants They assist and advise the chief of the service in the veterans hospital concerning organization, care of patients and appointment of residents and take a prominent role in the teaching of residents by ward rounds, seminars, clinics and demonstrations They are also available, to the hospital for consultation in all matters relating to their specialties as applied to the care and treatment of patients It is desirable that consultants be certified by their specialty board and be veterans of either World War I or World War II They must be approved by the Deans' Committee The number of visits is regulated by the needs of the particular hospitals The second group consists of younger physicians of proved ability who are members of medical-school staffs or have an equivalent standing in the practicing profession of the community These men are called attendings They actively participate in the care of patients by conducting ward rounds, performing operations and carrying out such other therapeutic measures as may be required They also assist and advise in the organization of services and take a prominent role in teaching residents The chief of the service delegates much of the care of the patients to these men The Veterans Administration, of course, is responsible for the care and treatment of patients, but the chief of service, as the representative of the Veterans Administration, delegates responsibilities according to the merits of the case The attendings participate in clinics, seminars and demonstrations and assume a great deal of the teaching load They must be certified by their specialty board, be veterans of World War II and be approved by the Deans' Committee The number of visits vary according to the needs of the hospitals

Physicians accepted for residency training must be graduates from approved medical schools and veterans of World War II, must have the intention and ability to go on to specialty-board certification and must be approved by the Deans' Committee

The Veterans Administration hospitals at present interested in the residency training program are those located in Bedford, Rutland Heights and West Roxbury The West Roxbury Hospital has been actively studied by the Deans' Committee, and a qualified staff has already been appointed It is anticipated in the near future that this hospital will have the approval of the various specialty boards as a suitable institution for residency training The newly appointed staff consists of the following physicians

CONSULTANTS

Dr C H Allman	Ear, nose and throat
Dr J C Amb	Endocrinology
Dr T L Badger	Chest diseases
Dr J S Barr	Orthopedic surgery
Dr H K Beecher	Anesthesia
Dr W M Daland	Plastic surgery
Dr W Dameshek	Hematology
Dr J G Downing	Dermatology
Dr J Homans	Vascular surgery
Dr T Lanman	Surgery
Dr J R Lingley	Röntgenology
Dr W A Messner	Pathology
Dr L Parsons	Gynecology
Dr F Rackemann	Allergy
Dr B Sachs	Ophthalmology
Dr G C Shattuck	Tropical medicine
Dr R Stetson	Medicine
Dr M Strock	Maxillofacial surgery
Dr G Taylor	Surgery of tumors
Dr R G Vinal	Rehabilitation
Dr S N Vose	Urology
Dr C Westelhoeft	Communicable diseases
Dr P White	Cardiology

ATTENDINGS

Dr D Adams	Medicine
Dr B Banks	Medicine
Dr N J Bakst	Medicine
Dr R H Betts	Thoracic surgery
Dr W Bloomberg	Neuropsychiatry
Dr T Botsford	Surgery
Dr W Buddington	Urology
Dr R Chute	Urology
Dr J Drockner	Ear, nose and throat

This program was inaugurated under the leadership of Reverend Russell L. Dicks, and it has been continued and finally organized into the present new institute under the immediate direction of Reverend Rollin J. Fairbanks, Protestant chaplain of the hospital. On the Board of Governors are represented theological schools, hospitals, the Massachusetts and Michigan councils of churches and the Ella Lyman Cabot Trust. Recently the University Hospital at Ann Arbor, Michigan, was selected as the Institute's second training center.

The purpose of the Institute, as set forth in its constitution, is "to organize, develop and support a comprehensive educational and research program in the field of pastoral care, with special reference to the sick, using the opportunities offered by clinical training as a primary means to this end." Pastoral care, it might be stated parenthetically, may be considered as the art of ministering to the individual—to care for like a shepherd in the spiritual sense, and if the Institute can achieve its goals, the preventive phase of pastoral care will also be fully developed.

For the summer of 1946 three training sessions are available—two at the Massachusetts General Hospital, limited to an enrollment of twenty men each, and one at Ann Arbor, where fifteen theological students or clergymen will be enrolled. The first two weeks of each six-week course are devoted by its participants to half-time work as orderlies on the hospital wards. Many clinical phases of hospital experience are observed, daily seminars are held, and lectures are given on pastoral, medical, psychiatric and social-service problems. At the end, the student, whether he be a young theologian or a minister with years of church work behind him, will have gained experience in human relations and will be better equipped to embark on or resume the pastoral work of his own parish.

It is heartening to realize that organized religion, without which the human community can hardly function properly, has not irrevocably jelled into any outworn form but has retained within itself the capacity of remolding its ministrations to fit the needs of human kind. It might be well if the student of medicine, at any stage in his life-long task of learning, could also visit for awhile with the pastor

and review the humble doctrines of ministering to the spirit. Each profession, indeed, assumes to no small degree the role of Knowledge in the moral play of "Everyman."

**Everyman, I will go with thee, and be thy guide,
In thy most need to go by thy side**

MASSACHUSETTS MEDICAL SOCIETY

SECRETARY'S OFFICE

PEPPER BILL (S 1318)

The following telegram was received on July 16 from Dr. Joseph S. Lawrence, director of the American Medical Association's Bureau of Information in Washington:

YESTERDAY JULY 15 FOLLOWING INSTRUCTIONS SENATE COMMITTEE EDUCATION AND LABOR SENATORS PEPPER AND TAFT INTRODUCED SENATE JOINT RESOLUTION 177 AMENDING TITLE 5 OF SOCIAL SECURITY ACT TO PROVIDE FOR INCREASED GRANTS TO STATES FOR MATERNAL AND CHILD HEALTH CRIPPLED CHILDREN AND CHILD WELFARE SERVICES STOP THE RESOLUTION WHICH IS TO SERVE AS SUBSTITUTE FOR PEPPER MATERNAL AND CHILD WELFARE BILL WAS REFERRED TO COMMITTEE ON FINANCE

MICHAEL A. TIGHE, *Secretary*

DISTRIBUTION AND SALE OF HEAVY CREAM

The following is submitted for the information of the readers of the *Journal*:

On June 26, 1946, the United States Department of Agriculture issued a directive (WFO 149, Part 1401-Dairy Products), which has to do with the distribution and sale of cream.

This directive, which became effective on July 1, 1946, prohibits the distribution and sale of cream, except to handlers, that is higher than 19 per cent in its fat content, except in those states in which the local law defines cream as containing a minimum of more than 19 per cent fat, 20 per cent being the maximum allowed.

The Massachusetts law requires that cream that is to be offered for sale within the confines of the Commonwealth shall contain 16 per cent fat as a minimum. Under this directive, the milk handlers in Massachusetts may therefore offer for sale only cream that is not in excess of 19 per cent fat, subject to the following exceptions:

- 1 Any person may sell or deliver to or for any patient, or to any establishment engaged in the care and treatment of the sick, cream of such milk fat content, and in such quantities, as may be necessary for supervised medical treatment of such patient or the patients of such establishment.

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SCHISTOSOMIASIS JAPONICA

Diagnosis and Treatment in American Soldiers

MAJOR PORTER K. MASON, M C, A U S, COLONEL WORTH B. DANIELS, M C, A U S,
CAPTAIN FRANKLIN K. PADDOCK, M C, A U S, and MAJOR HARRY H. GORDON, M C, A U S

FOLLOWING the invasion of Leyte, an island in the Philippines, on October 20, 1944, cases of schistosomiasis japonica began to appear among Army personnel. It is the purpose of this report to describe briefly the results of an investigation of 481 patients studied four to nine months after acquiring the disease. The dissemination of this information will enable patients from this and other hospitals who are being discharged from the Army and scattered throughout the country to obtain appropriate care in places where the disease is unknown. Although the results of this study are to be reported separately in considerable detail,¹ it is believed that the information acquired concerning diagnosis and treatment merits wider distribution. Since up to the present no snail capable of acting as an intermediate host for the parasite has been found in the United States,² it is not expected that the disease will be disseminated in this country. The problem therefore resolves itself into one of assuring proper care and follow-up for the small number of soldiers already infected.

THE ACUTE ILLNESS OVERSEAS

Several weeks after exposure, the patients developed chills, sweats, generalized malaise, lethargy, headache, anorexia, mild diarrhea and abdominal pain, with marked weight loss. Urticaria and jaundice were observed in some cases. Examination revealed a slightly enlarged and tender liver and occasionally an enlarged spleen. Leukocytosis with marked eosinophilia was usual. In some asymptomatic cases suspected of the disease because of eosinophilia, the ova of *Schistosoma japonicum* were found in the stools. In 8 of the 481 patients considered at this hospital to have had schistosomiasis japonica, there were weakness of the extremities and reflex abnormalities that followed an encephalomyelitis in the acute phase of the disease.

In about three fourths of the patients the ova of *Schistosoma japonicum* were found in the stools.

Fuadin was given to almost all the patients treated overseas, the usual amount given being approximately 40 cc. In some cases a second course of the drug was given. Tartar emetic, in a concentration higher than that employed at this hospital, was used in a small number of cases.

THE DISEASE AS SEEN IN THE UNITED STATES

Four to nine months following their acute illness, patients were evacuated to this country for further study. On arrival at this hospital, they were convalescent and did not appear ill. The only abnormalities that appeared to have some specificity were recurrent cramps and tenderness in the upper abdomen. A slightly enlarged liver was felt in 10 per cent of the patients.

During the period of observation here, which lasted for three months or more, the patients tended to improve clinically whether or not their stools were demonstrated to contain ova. On discharge almost all the patients were free of signs and symptoms of the disease and had no disability preventing unlimited activity. They were advised, however, to have their stools examined every three months for a period of one year for reasons given below.

EXAMINATION OF STOOLS

The stools were examined over a period of at least two weeks initially and after two furloughs of thirty and twenty days, respectively. Patients untreated at this hospital because of repeatedly negative stools were released after an average of twenty-two stool examinations over a period averaging four months.

Methods

Stools were examined in all patients by multiple direct smears and in some by concentration methods. Although multiple direct smears detected the vast majority of positive stools, in a small number one or another of the sedimentation methods was necessary.

Dr W Elliston	Orthopedic surgery
Dr J E Flynn	Surgery
Dr J Frazee	Ear, nose and throat
Dr I H Jaffee	Medicine
Dr K B Lawrence	Surgery
Dr W F Leadbetter	Urology
Dr E H Lewis	Anesthesia
Dr J Messina	Dermatology
Dr L Pilcher	Surgery
Dr L Souther	Surgery
Dr J Stillman	Medicine
Dr G L Sullivan	Ophthalmology
Dr A Thibodeau	Orthopedic surgery
Dr T Urmey	Medicine
Dr J Townsend	Medicine
Dr W R Wegner	Neurosurgery

RESIDENTS

Dr D V Baker	Surgery
Dr W J Baker	Surgery
Dr V B Ballard	Medicine
Dr R E Barkin	Medicine
Dr C D Beheher	Surgery
Dr M Blum	Medicine
Dr J S Chambers	Surgery
Dr H R Clement	Medicine
Dr J F Cooper	Surgery
Dr R Evans	Medicine
Dr A Finck	Surgery
Dr D Freni	Surgery
Dr R Grissom	Surgery
Dr J W Hartshorn	Surgery
Dr G V Leveault	Medicine
Dr S Levine	Medicine
Dr S Manelian	Orthopedic surgery
Dr R L Ohler	Medicine
Dr M H Rose	Medicine
Dr L Ryack	Medicine
Dr R Vaughn	Surgery
Dr G Warren	Urology
Dr A S Zdanis	Medicine

In addition to the above appointments the following physicians have accepted full-time positions in the Veterans Administration and have been assigned to the West Roxbury Hospital

Dr John Houghton	Chief of pathology
Dr D Littman	Cardiology
Dr John Poutas	Clinical director
Dr J L Rudd	Physical medicine and rehabilitation
Dr Samuel Tartakoff	Chief of neuropsychiatry
Dr Richard Warren	Chief of surgery
Dr Thomas Warthin	Chief of medicine
Dr Egon Wissing	Chief of roentgenology

Preliminary studies have been made of the needs of the Neuropsychiatric Hospital at Bedford. The Neuropsychiatric Subcommittee, consisting of Dr Harry Solomon, of Harvard Medical School, chairman, Dr William Malamud, of Boston University School of Medicine, and Dr Clifton Perkins, State Commissioner of Mental Diseases, is at present formulating plans for training at Bedford. The following part-time physicians have been appointed to the staff at Bedford: Dr Douglas Thom, consultant in neuropsychiatry, Dr Sylvester B Kelley, consultant in urology, and Dr Jackson Thomas, attending in neuropsychiatry. Dr Norman Elton is chief of pathology and a full-time Veterans Administration appointee. As the needs are more fully ascertained, more part-time appointments will be made and residents will be assigned.

The tuberculosis hospital at Rutland Heights is also under study. Up to the present time little change has been made other than the appointment of Dr L Davenport as consultant in chest diseases and of Dr D Harken as consultant in thoracic surgery.

The Cushing General Army Hospital at Framingham will be taken over by the Veterans Administration on October 1, 1946. The program that has been carried out at the West Roxbury Hospital will be put into effect. It is anticipated that this hospital will have 1000 beds, which will provide many openings for consultants, attendings and residents.

The Dean's Committee is happy to report that it has had excellent co-operation from the Veterans Administration and from the physicians of the region. There is every reason to believe that this program will, as it develops, ensure that the veteran will receive the best available quality of medical care and that it will also provide an excellent opportunity for residency training leading to certification by the various specialty boards.

DALE FRIEND, Secretary

Harvard Medical School
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Psychology of Women. A psychoanalytic interpretation. Volume II *Motherhood*. By Helene Deutsch, M.D., associate psychiatrist, Massachusetts General Hospital, and lecturer, Boston Psychoanalytic Institute. 8°, cloth, 498 pp. New York: Grune and Stratton, 1945. \$4.50.

In this second volume Dr Deutsch has completed her work on the psychological life of the normal woman and discusses all the aspects of motherhood.

Local Health Units for the Nation. A report. By Hare Emerson, M.D. With the collaboration of Martha Lubitbuhl, M.A. 4°, paper, 333 pp., illustrated. New York: The Commonwealth Fund, 1945. \$1.25.

This monograph is a report by a committee of state and local public-health administrators whose purpose was to suggest the way to cover a free society with full time health services at the community level.

Fundamentals of Pharmacology. By Clinton H. Thielen, M.D., Ph.D., professor and head of the Department of Pharmacology, School of Medicine, University of Southern California, and attending pathologist (toxicology), Los Angeles County Hospital. *Medical Students Series* 8°, cloth, 497 pp., with 36 illustrations and 19 tables. New York and London: Paul B. Hoeber, Incorporated, 1945. \$5.75.

This new manual in the *Medical Students Series* is a practical and concise text for students and physicians. It contains the essentials of pharmacology brought up to date and correlated with modern therapeutics. Despite its conciseness, valuable clinical material has not been omitted from the text. The author makes use of a simple original classification, discussing in order drugs acting on the central and peripheral nervous systems, those acting on the muscular system, antiparasitics, hormones, iron, tissue extracts, vitamins and drugs having local action on body surfaces, including irritants, cathartics, expectorants and emetics, carcinatives, emollients and demulcents, astringents and antacids. There are also short chapters on chemical diagnostic agents, drug action on cells, pharmaceutical preparations and prescription writing.

All important U.S.P. preparations are described, and a sufficient description of the physical and chemical properties of drugs is given to facilitate writing prescriptions. The major emphasis is laid on the dynamics of drug action, the absorption, distribution, metabolism and excretion of essential drugs and their therapeutic indications.

The text is well written and printed on good paper, with a good type, and a comprehensive, inclusive index ends the volume. The book should prove useful as a ready reference source in its field.

NOTICES

ANNOUNCEMENTS

Dr William B. Coen announces the removal of his office to 111 Maple Street, Springfield.

Dr Armand M. Gamboa announces his return from naval service and the opening of his office at 1075 Boylston Street, Boston.

Dr Nelson R. Saphir announces his return from military service and will resume the practice of internal medicine at Suite 3, Hotel Canterbury, 14 Charlesgate West, Boston.

(Notices continued on page x)

clude its use. Much of this result may be due to too rapid injections or too high a concentration of the solution used. This conclusion is based on the insignificance of toxic reactions found in this study under the conditions outlined below.

With a dilute solution (0.5 per cent) and a slow rate of injection (8 cc a minute), reactions sufficiently severe to justify stopping the drug were encountered in only 2 of the 102 patients treated with more than two thousand injections and carefully observed for evidence of reaction. Seventy-one per cent at one time or another developed a transient hacking cough. Nausea, occasionally associated with vomiting, appeared in 15 per cent. In most cases, the nausea could be diminished by having the patient suck a piece of lemon during the injection. The most striking toxic reaction was a transient sense of soreness, usually in the region of the shoulders, which appeared eight to twelve hours after the injection in 75 per cent of the cases. It did not prevent the patients from being ambulatory.

In all the patients treated with tartar emetic and in half of those treated with fuadin, there appeared a diminution in the size of the T waves in one or more leads of the electrocardiograms, with a complete inversion in some cases.¹⁰ On casual examination these changes were like those seen in coronary thrombosis or pericarditis. With cessation of therapy, the T waves returned to normal. These changes were never associated with any clinical signs or symptoms of cardiac disease, and the drug was not stopped.

Some evidence has been obtained that antimony causes a minor transient impairment of liver function.⁵ It is therefore suggested that in patients who require repeated treatment with antimony compounds, tests of liver function should be performed before, during and after the administration of therapy to determine whether there is any cumulative toxic effect.

No deleterious effect of antimony was noted in the urine or in the cellular constituents of the blood.

Results

One hundred patients with ova of *S. japonicum* in the stools were treated with either fuadin or tartar emetic. The cases were alternated without regard to overseas therapy or to the patients' condition overseas or on arrival here. Additional patients were treated with longer courses of fuadin (105 cc) and tartar emetic (416 cc) at the same individual dose level. These patients are now being followed at another hospital.

After the completion of treatment, the patients were sent on a thirty-day furlough. On their return, follow-up studies were begun. An average of nineteen stools were examined over an average period of three and a half months following treatment before therapy was considered successful. Any patient whose stool was found to be positive at any time

during the follow-up period was given the same course of treatment again and was similarly followed.

The rate of apparent cure (negative stools) in the tartar emetic group was 81 per cent, whereas that for the fuadin group was 18 per cent. In addition, of the 16 cases treated twice with fuadin at this hospital because of continued positive stools and followed for a short period of time, 69 per cent had positive stools for the third time.

Discussion

Schistosomiasis japonica as encountered in these patients offered a unique group for study. The usual textbook picture of this illness is based on the cases in which there has been repeated exposure over a period of years, whereas in this series the maximum length of exposure was only a few months. Furthermore, these patients were healthy soldiers who were given the advantages of prompt treatment.

The most frequent complication in the often exposed native population, owing to the deposition of the eggs, is said to be hepatomegaly and splenomegaly.⁷ In the present series there was little evidence of such changes. Recurrent epigastric pain and tenderness appeared to be the most frequent symptom after the acute phase had subsided, but on discharge there was no evident disability. Whether definite liver disease may develop later if ova continue to be produced is not known. Asymptomatic infections also occurred. Certainly, the possibility should be kept in mind in all persons who were on the east coast of Leyte or in other endemic areas.⁶

Frequent stool examinations by more than one method are required to demonstrate the eggs in the stools. From these studies it is obvious that an occasional observation is insufficient. It is only by repeated stool examinations with multiple methods that eggs will be demonstrated, their discovery leading to the institution of therapy.

Treatment at this hospital with tartar emetic showed better results than did that with fuadin. Furthermore, the toxic symptoms of tartar emetic were for the most part mild. Since, however, the sole criterion of cure is the absence of eggs in the stools, no final conclusion can be drawn until these cases have been followed for many years. Our arbitrary recommendation of one year of follow-up may require alteration in the light of continuing collection of data.

Many of the soldiers showed anxiety about the possibility of developing disability at a later date. Intelligent reassurance can be based only on the taking of steps to guarantee them adequate re-examination and treatment in both the Army and civilian life. It is the purpose of this paper to call attention to this need.

SUMMARY AND CONCLUSIONS

Four hundred and eighty-one cases of schistosomiasis japonica acquired on Leyte, an island in

for detection of the ova. When a modified gravity sedimentation method was made available,³ it was found in a comparative study to add a significant number of positive results.⁴

In the direct smear method, a bit of mucus is taken from the outside of the stool, as being likeliest to contain eggs. This is mixed with a small amount of tap water and mounted under a coverslip. Search of the entire covered area is made through the low-power lens of the microscope, and any suspicious objects are examined under the high-dry lens. Eggs were in most cases readily distinguished under low power. Even under high power, the single laterally placed knoblike spine was rarely seen. Motion of the miracidia could be seen in viable eggs.

In the modified gravity sedimentation method of Barody,³ approximately 5 gm of feces is partially emulsified in 35 cc of tap water by shaking in a 100-cc test tube. The fluid is strained through a single layer of surgical gauze into a 30-cc centrifuge tube and centrifuged at 1000 r p m for one minute. The supernatant fluid is discarded and the sediment is resuspended in tap water. Centrifuging is repeated three or four times until the supernatant fluid is relatively clear. A portion of the final sediment is transferred to a slide, covered and examined microscopically.

Results

Thirty-one per cent of all patients admitted to this hospital with a diagnosis of schistosomiasis japonica had eggs in their stools, and the results of stool findings overseas combined with those obtained here proved conclusively that 80 per cent of these patients had schistosomiasis. In the remainder the clinical history was sufficiently characteristic to warrant little doubt of the diagnosis.

In approximately 10 per cent of the cases found to be positive here, the eggs were not found until the final follow-up period, when a minimum of twelve stools had been examined. In some cases, more than twenty stools were examined before ova were found.

An eosinophilia of 10 per cent or more was found in half the cases on admission here and was associated with the finding of ova in the stools two or three times more frequently than when the eosinophilia was less than 10 per cent. During the follow-up periods, however, an eosinophilia of more than 20 per cent was occasionally encountered even in the cases with repeatedly negative stools. Although not of specific diagnostic value in schistosomiasis because of its presence in other parasitic infections, a persistent eosinophilia demands an even more meticulous search for schistosome eggs.

A variety of liver-function tests done on initial examination showed a 10 per cent incidence of mild impairment.⁵ There was no apparent relation between these abnormalities and the stool findings.

Sigmoidoscopy was done routinely in the first 300 patients. Abnormalities were found in only 3

patients. Since the stools of these patients contained ova on direct examination, this procedure was not helpful in making the diagnosis. Barium enemas in 50 cases were normal.

Of the stools of 463 patients evacuated with a diagnosis of schistosomiasis japonica, those of 146 (31.5 per cent) showed one hundred and seventy-eight infections with seven species of pathogenic intestinal parasites. The incidence of infection in these 146 patients was as follows: hookworm, 16.4 per cent, trichocephalus, 11.4 per cent, *Endamoeba histolytica*, 3.5 per cent, *Ascaris lumbricoides*, 3.2 per cent, Strongyloides, 2.2 per cent, *Hymenolepis nana*, 1.1 per cent, and *Giardia lamblia*, 0.6 per cent.

TREATMENT

The incidence of the failure of treatment as judged by the finding of positive stools in patients treated overseas was found to be definitely lower with tartar emetic than with fuadin. Treatments with these two drugs at this hospital were also compared.

Fuadin

- Fuadin, a trivalent antimony compound, was given in 6.3 per cent solution intramuscularly. Initial doses of 1.5, 3.5 and 5.0 cc were given on successive days, followed by injections of 5.0 cc every other day until a total of 65 cc (0.57 gm antimony) had been given, which required twenty-five days.⁶

Commercial Tartar Emetic

Commercial tartar emetic, also a trivalent antimony compound was given intravenously in the form of a 0.5 per cent solution in 5 per cent dextrose in normal saline solution at a maximum rate of 8 cc a minute. The patient was required to lie down during the injection and for one hour after it. The drug was given every other day. The initial dose was 8 cc, this was increased by 4 cc with each dose until a level of 24 cc was reached. Thereafter 24 cc was given every other day until a total of 320 cc (0.58 gm of antimony) had been given, which required twenty-nine days.

Freshly Prepared Tartar Emetic

Freshly prepared tartar emetic was used as follows. Sufficient potassium and antimony tartrate was accurately weighed with a sterile technic to make a solution of 0.5 per cent in 5 per cent dextrose in normal saline solution. After the solution was prepared, it was heated in a boiling hot-water bath for five minutes and allowed to cool prior to administration. The solution was injected at the same rate and in the same amounts as was the commercial tartar emetic.

Evidence of Toxicity

Judging by the literature⁷ and by certain reports from the Pacific,^{8,9} toxic reactions due to intravenous tartar emetic may be of sufficient severity to pre-

From September, 1943, to the present time there was shipped a total of 698,973 tons of medical supplies, kits, chests and other medical items. In normal times such an operation represents a big job. In wartime, with shortages of many items needed for the production of these supplies and the difficulties in getting the goods transported, the job was accomplished only by fighting every ton of equipment almost every mile of the way from the raw material to medical aid for a wounded man.

Penicillin is a good illustration of the problems that confronted us. Prior to 1943 the world had produced a total of only 1 pound of penicillin. Early in 1945 the original goal of 300,000,000,000 units a month, or 15 pounds a day, was passed. The original price of \$20 a vial was cut to the present figure of approximately 76 cents.

Atabrine was another source of worry. The Allied Nations lost 95 per cent of the world's supply of quinine when the Japanese captured the Netherlands East Indies. Like penicillin, atabrine also introduced what seemed like insurmountable obstacles in the intricate process of manufacture. It takes $2\frac{1}{2}$ tons of chemicals to make 100 pounds of atabrine, a ratio of 30:1. On the surrender of Corregidor there were 35,000,000 tablets on hand and a yearly manufacturing capacity of 227,000,000 tablets. Through heavy pressure from the Medical Department production was boosted so that 3,500,000,000 tablets were produced in 1944, with the cost brought down from \$24 per 1000 tablets in 1940 to \$3 in 1944.

Blood plasma is an interesting item from a supply standpoint. The processing of blood plasma began in February, 1941. Procurement averaged approximately 140,000 units of 250 cc per month, with an all-time high of 178,000 in October, 1944. Shipments of whole blood to Europe started in August, 1944, and continued until May, 1945, with a total shipment of 206,000 pints of Group O blood. To the Pacific, 177,734 pints were flown.

It was through the success of our operations in supply and personnel that we were able to staff, equip and maintain the system of Army hospitals. Overseas in all theaters there were 217 general, 196 station, 99 field, 91 evacuation and 73 portable surgical hospitals. Including convalescent hospitals and centers, there was a total of 692 hospitals overseas at the peak of operations. There were 65 general and 13 convalescent hospitals in the Zone of the Interior. During the war 15,000,000 patients were admitted to Army hospitals for treatment. The peak of the world-wide total load was 544,000 in April, 1945. The peak in Army hospitals in this country was 312,000 in August, 1945.

The American Army in this war was the healthiest in the world. The program of preventive medicine was an important factor in this record. Through the development and use of toxoids and vaccines, fear of tetanus, yellow fever and typhus became

a thing of the past. There were no deaths from these diseases among American soldiers who were inoculated against them.

Malaria at one time incapacitated ten times as many soldiers as did Japanese bullets. Through proper control measures malaria was cut to one fourth its incidence in the early days of the war in the Pacific. Atabrine proved even more satisfactory than quinine. It serves as a suppressive just as quinine does, and also cures the malignant form of disease known as falciparum malaria. The part DDT played in the battle against disease was, of course, a major one. In my tours to overseas theaters I have seen islands, such as Saipan, where there were no traces of mosquitoes or flies as a result of the spraying of DDT from airplanes.

Preventive measures also played a large part in cutting down casualties in the Air Force. As air surgeon of the Eighth Air Force, Brigadier General Malcolm C. Grow worked out a system of rest camps, the spacing of missions farther apart and the establishment of a definite number of missions that when completed would end the flier's tour of duty in that theater. These antifatigue measures proved highly effective in combating this problem among fliers.

To be certain that aviators had sufficient oxygen they were given courses of instruction in handling personal equipment, and "personal officers" were appointed to see that all missions were started with equipment in proper order. Heaters were developed to cut down the freezing of oxygen masks. These same officers checked clothing and equipment to guard against frostbite and instructed fliers how to prevent it. Engineers were instructed to keep the waist windows in the fuselage closed.

The field of medicine has also proved rich in results in this war. The death rate from disease was only 0.6 per 1000 men per year, as against 16.5 in the last war. The pneumonia rate was cut from 24 in the last war to 0.6, and that of meningitis was lowered from 38 to 4. Days lost due to venereal disease amounted to 47 per case in 1937, whereas last year the days lost per case totaled only 5.

Great advances were made in the adaptation of civilian to military surgery in this war, and improvements in both will be noted in the future from the facts that were learned. A great deal is owed to Colonel E. D. Churchill, surgical consultant in the Mediterranean Theater, for his development and standardization of wound management and resuscitation.

Surgical care has been divided into three echelons. The initial or primary echelon is in forward hospitals, where the wound is thoroughly debrided, left open, immobilized by plaster or splints and made ready for transportation to fixed hospitals in the rear. Resuscitation is necessary at this echelon of treatment. Most of these patients are in shock, and many have lost much blood. Plasma prevented

the Philippines, were studied at an Army general hospital in the United States

Recurrent epigastric cramps and tenderness were the most frequent complaints on admission, but in almost all cases these had disappeared by the time of discharge

Repeated stool examinations by more than one method were necessary to demonstrate the eggs of *Schistosoma japonicum*. A persistent eosinophilia was suggestive but not diagnostic of continued activity of the disease

On the basis of comparable series, treatment with tartar emetic was found to be much more effective than that with fuadin. Significant toxic reactions with tartar emetic were rare

It is urged that stool examinations be done repeatedly and by multiple methods on men who have

been exposed to this disease so that treatment may be instituted if ova are found

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WARTIME ACTIVITIES OF THE ARMY MEDICAL DEPARTMENT*

MAJOR GENERAL NORMAN T. KIRK†

IT IS a distinct privilege to be present at this annual meeting of the Tufts Medical Alumni Association. I look back with pleasant memories to about a year ago when I was present at the commissioning exercises of the graduating class of Tufts College Medical School and also those of Harvard and Boston universities. I thoroughly enjoyed renewing old acquaintances and making new friends on that occasion, and I am happy to be with you again tonight.

I am aware of the great contribution that the Tufts Medical Alumni Association and the Tufts College Medical School have made in this war. Some of you may not realize just how close my contact is with your institutions. The office on my immediate left is occupied by the deputy surgeon general, who is Brigadier General Raymond W. Bliss, a Tufts alumnus of the Class of 1910, and the office on my immediate right is that of the executive officer, Colonel Robert J. Carpenter, a Tufts alumnus of the Class of 1914. With an enthusiastic and loyal Tufts alumnus on either side, I think you can understand how I happen to be fairly well informed on your activities.

Tufts College Medical School has a rich heritage, dating back for over half a century, of providing New England and other sections of the country with high-type general practitioners. You have followed a policy of keeping in close touch with your alumni to see that they have kept abreast of modern practices. You have not overlooked the specialties, of course, but you have particularly stressed a program of developing to the highest professional

standards your training of the general practitioner. In this day of specialization I am glad to see that your institution has not overlooked the fact that there is still a definite need for general practitioners in the rural sections.

I realize that everyone in this audience has played an important part in recent years, whether he served in uniform or remained to do the vitally necessary tasks in civilian practice or as part of the staff of Tufts College Medical School. You have contributed more than your share, and I think that you will be interested in hearing something of the overall story of the Army Medical Department's activities in the war. Now that it is over, I can give you a more intimate glimpse into what was done by this department since the start of the emergency.

You know that we had to start practically from scratch. In the Regular Army there were only about 1200 medical officers. In planning an organization geared to the medical needs of an army of 8,000,000, you can see what they meant. Largely because of the foresight and loyalty of professional men of your type, we had a reserve that helped us bring the strength of the Medical Corps to approximately 47,000 at the peak of the war. In addition, there were 15,000 officers in the Dental Corps, 2000 in the Veterinary Corps, 2000 in the Sanitary Corps, 61 in the Pharmacy Corps and 18,700 in the Medical Administrative Corps. The total number of nurses reached approximately 57,000, and there were 535,000 enlisted men trained as medical-aid men, technicians, litter bearers, ambulance drivers, clerks and so forth. The entire Medical Department had to be expanded from a skeleton organization into a full-blown medical machine, which did the biggest job ever performed by American medicine.

*An address delivered at the annual meeting of Tufts Medical Alumni Association, Boston, April 10, 1946.

†Surgeon General, United States Army.

that our task has been finished On March 1, 1946, there were 129,000 patients in Army hospitals, 60,000 of these being evacuees from overseas You can see that we still have a sizable job on our hands In addition, the Medical Department must lay its plans for the interim and postwar care of the Nation's soldiers One important phase of this will be to secure a sufficient number of specialists for the Regular Army and Reserve Corps

Here is where your organization can continue to help in the same grand way that you have in the past Tufts Medical Alumni Association and Tufts

College Medical School will continue to merit the deep appreciation of the Medical Department by giving their full support to the building of a strong Medical Reserve Corps On behalf of the Army Medical Department, I express our sincere gratitude for what you have done, and judging by your members whom I know and the record of your past performances, I am certain that we can count on your unswerving and loyal support in our future plans for the type of Medical Reserve Corps that this country should and must have

SCURVY*

A Survey of Two Hundred and Forty-One Cases

IHSAN DOGRAMACI, M D †

ST LOUIS, MISSOURI

SCURVY is still a reasonably frequent disease in pediatric practice This is a disquieting fact that should cause concern to all responsible for the

At least 241 clinically typical cases of scurvy were seen in these hospitals during the last ten years, according to the lists of the Record Library The cases

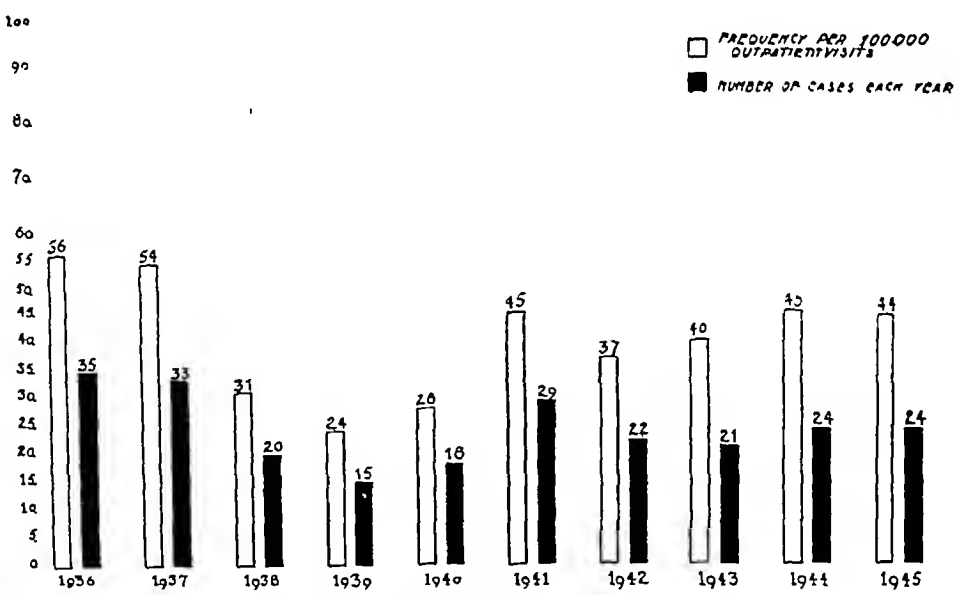


FIGURE 1 Morbidity of Scurvy from 1936 to 1945

health of infants, inasmuch as the disease can so easily and effectively be prevented The purpose of this report is to place on record the large number of cases seen in the Infants' and Children's hospitals during the last decade, to analyze the causes of inadequate intake of ascorbic acid and to suggest measures possibly leading to a decrease of the incidence of scurvy

with insufficient data were not included in this report

The criteria used in selecting the cases were two-fold First, all the selected cases had a history of inadequate vitamin C intake or some of the symptoms and signs characteristic of the disease, listed in Tables 1 and 2 Second, the diagnosis was verified in each case by roentgenograms and in a few cases by laboratory measurements or by the rapid therapeutic effect of vitamin C The roentgen-ray evidence of the changes in the long bones included some

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the loss of many lives after injury and previous to arrival at a hospital for surgery. It was soon demonstrated that plasma alone was not sufficient to permit life-saving surgery and must be supplemented by whole blood.

In the second echelon, intermediate or reparative surgery is carried on at the fixed hospital in the rear. Here, plaster and splints are removed, secondary closure is accomplished by plastic procedures or by skin grafts, and fractures of long bones are placed in suspension traction until consolidated and then fixed in plaster for transportation to the Zone of the Interior. Soft-tissue wounds heal much earlier under these procedures, and the soldier is returned to duty in the theater in a much shorter period of time. Compound fractures are converted into simple fractures, and the patients arrive home without osteomyelitis and with advanced union. Patients with colostomies that were performed as a life-saving measure when initial surgery was done are prepared for evacuation to the Zone of the Interior or the colostomy is closed in the theater. Thoracotomy for the removal of blood clot or foreign bodies becomes routine, and many of these patients return to duty in the theater instead of returning home with a drainage tube in the chest, with chronic empyema and marked loss of weight, and requiring extended hospitalization. Penicillin and sulfonamides aid materially in the prevention and control of infection, but they are adjuncts only to good surgery.

The third echelon is definitive or reconstructive surgery—mainly practiced in the Zone of the Interior and at times in the Zone of Communications. Here plastic procedures on skin, nerve, bone and vessels and other procedures are carried on to correct the defect, mobilize joints and prepare the patient for return to the Army or to civil life.

Surgery was an important factor in the following results, which will be of interest to you. Of 598,000 soldiers wounded in this war, approximately 96 per cent who reached Army hospitals lived, 26,600 dying of wounds, 376,000 were returned to duty in the theater, and an additional 55,200 were returned to duty in the United States. One hundred and ten thousand were returned to civilian life with a certificate of disability discharge. There are approximately 30,200 of these patients still receiving treatment in general hospitals here at home. These sick and wounded soldiers received the best medical care as a result of the system of specialized centers that the Army established in general hospitals. There were not enough specialists, so the Army brought the patients to the specialists. The following centers were established for specialized care: seven amputation centers, nineteen neurosurgery centers, five thoracic-surgery centers, eight plastic-surgery centers, two ophthalmologic-surgery and blind centers, three deaf centers, nine deep x-ray-therapy centers, three radium-therapy centers, three vascular centers, nineteen neurology centers,

two arthritis centers, seven centers for syphilis of the central nervous system, two tuberculosis centers, two rheumatic-fever centers and two tropical-disease centers.

An example of how this specialized-center system worked out is afforded in the treatment of paraplegic patients. They are small in numbers,—only about 1400 in all—but the Army has devoted the same amount of effort to helping them as in the case of patients in larger groups. In fact, the results in these cases have surpassed anything in the previous history of neurosurgery and constitute a tribute to the professional competence of the Army doctors in this war. Until this program was instituted, men with spinal-cord injuries and resulting paralysis were regarded as hopeless invalids and, I fear, were treated as such. This attitude has been completely reversed by the Army Medical Corps, which met the problem with all the resources of the profession.

Prompt and skilled surgery was the first step in the treatment of these cases. Nutritionists and dietitians helped to restore underweight patients, who were evacuated to one of the nineteen neurosurgical centers. The next phase of treatment was largely urologic, and a urologist was in constant attendance. Decubitus ulcers were closed by surgery, either by skin grafting or by plastic procedures. Finally came the matter of ambulation. We did not deceive ourselves about this. Ambulation as you and I understand the term is beyond the capacity of all but the incomplete paraplegic patients, but ambulation in the sense of getting about with the aid of braces and crutches sufficiently well to care for oneself is a definite possibility in most patients with cord lesions at or below the tenth dorsal vertebra and is a more guarded possibility in cases with lesions below the second dorsal vertebra. In patients with lesions above this level ambulation is not possible, but a wheel-chair existence is. In other words, so far as this program was concerned, a bed-ridden patient was simply not conceived of. When a man reached a paraplegic center it was taken for granted that he would be out of bed promptly or at least as soon as certain physical deficiencies had been corrected and that he would attempt to walk with equal promptness. An unexplained improvement always occurs when these patients begin to move about. The surprising results we have realized in a majority of the cases have been against untold odds through the untiring and united efforts of neurosurgeons, plastic surgeons, orthopedic surgeons, urologists, internists, nutritionists, nurses, dietitians, physical therapists and hospital corpsmen. These results reflect the value of the specialized centers.

* * *

Most of what I have said refers to the work during the war, but I do not want to leave the impression

blood was present in the stools of 6 patients, whereas in the remaining 2 cases it could be detected only by the guaiac test. Gross hematuria was observed in 1 case, and microscopic hematuria in 3 cases.

The temperature was elevated in 40 per cent of the 228 cases in which it was recorded. In 65 per cent of all febrile cases no associated infection could

TABLE 2 Physical Signs on First Physical Examination (241 cases)

PHYSICAL SIGN	No OF CASES	PERCENTAGE
Tenderness in one or both lower or upper extremities	199	83
Enlarged costochondral junctions (rosary)	161	67
Involvement of gums	88	36
Swelling of one or both lower or upper extremities	26	11
Petechiae or ecchymoses (excluding ecchymosis of eyelids)	25	10
Ecchymosis of eyelids	8	3
Blood in stool	8	3
Blood in urine	4	2
Exophthalmos	3	1
Tenderness of ribs	2	—
Subconjunctival hemorrhage	1	—
Hemorrhage in retina	1	—
Hematoma (head)	1	—

be demonstrated, the fever apparently being related to the scurvy. An increased susceptibility of scorbutic patients to infection³ was confirmed in this survey. Thirty patients (12 per cent) had concurrent infections of the upper part of the respiratory tract. This means that the incidence of infection of the upper part of the respiratory tract was at least five times as high in the patients with scurvy as in the total number of all patients admitted to the Outpatient Department over the same period of time. Thirty-one patients (13 per cent) had miliaria, and an equal number had amoniacal dermatitis. The incidence of rickets was high, this symptom appearing in 22 patients (9 per cent). Anemia was also a relatively frequent finding, 12 per cent of all patients having an appreciable degree of anemia, usually of the hypochromic type. Six patients (2 per cent) had had pertussis at some time before the onset of scorbutic symptoms. Five patients (2 per cent) had definite signs of pneumonia when admitted to the hospital, in addition to frank evidence of scurvy.

The following case was particularly interesting in that scurvy simulated pneumonia.

R S, a 7-month-old boy, was admitted because of a generalized rash and crying for the 3 weeks prior to entry. He had not been receiving adequate amounts of vitamin C. Shortly before entry the gums became swollen and developed purplish areas anteriorly.

Physical examination revealed a well developed and well nourished pale, slightly cyanotic infant lying apathetically, with the legs held in the so-called "frog's leg" position and the right arm outstretched. The temperature was 101°F. The respirations were rapid, shallow and slightly irregular, with occasional cough. A macular rash was present over the anterior thorax, abdomen and lower legs, some of the lesions had brownish crusts, and many were petechial. Both eardrums were full and injected. The upper and lower gums were swollen, spongy and livid, with small petechial hemor-

rhages visible anteriorly. The pharynx and tonsils were reddened. The lungs contained a few scattered rhonchi. The legs were swollen and tender, and there was considerable beading of the costochondral junctions. The hemoglobin was 49 per cent, the red-cell count 3,460,000, and the white-cell count 15,700, with 75 per cent neutrophils. Blood Wassermann and tuberculin tests were negative, a throat culture was noncontributory, and urine examination was within normal limits. The plasma ascorbic acid level was zero. Roentgen-ray examination of the long bones showed advanced active scurvy.

It was thought that in addition to scurvy the patient had pneumonia, and he was placed in an oxygen tent. Because of the moderate anemia and the patient's acutely ill appearance, blood was transfused the day after entry. In spite of the giving of oxygen, the respirations continued to be rapid and the cyanosis persisted. Roentgenograms showed no evidence of pneumonia, and it was thought that the respiratory difficulty might be a manifestation of the so-called "cardiorespiratory symptom of scurvy" and he exaggerated by excessive pain and tenderness of the ribs. Accordingly, morphine was given in regularly repeated doses. This resulted in prompt relief, including disappearance of the cyanosis.

From 4 to 8 ounces of orange juice was administered daily. No chemotherapy was instituted. The rhinitis persisted and the inflammatory process in the ears did not subside. Paracentesis was done in the 4th week, with release of pus from the right middle ear and the patient was discharged free from symptoms 32 days after entry. During the last week, the temperature remained normal. Roentgenograms of the long bones taken shortly before discharge showed signs of healing scurvy.

ROENTGEN-RAY FINDINGS

In 127 of 133 cases examined roentgenologically, bone changes characteristic of scurvy were found. In 4 cases the changes were minimal but suggestive, whereas in the remaining 2 cases the findings were equivocal.

LABORATORY DATA

In 24 cases fasting plasma vitamin C levels were determined (Fig 4), and a mean value of 0.087 mg of ascorbic acid per 100 cc with a range of 0.0 to 0.3 mg was found. The mean value for normal infants with adequate nutrition is between 0.8 and 1.4 mg.⁴ Although low plasma vitamin C concentration value is a constant finding in untreated scurvy, it is by no means a certain indication of vitamin C depletion.⁵ Butler and Cushman's⁴ method of analysis of the whole blood and the white cells and platelets is recommended to obtain a more reliable index of vitamin C deficiency.

In 7 patients showing low values of ascorbic acid in the plasma and its absence in the urine, large doses of crystalline ascorbic acid were administered over several days, and vitamin replenishment was accomplished quickly or over a longer period of time, depending primarily on the dose of ascorbic acid employed.*

The serum alkaline-phosphatase level was measured in 26 scorbutic patients, and the results were found to be abnormally low. In 1 patient the phosphatase value was 0.19 Kay units (the value for a normal infant of the same age is 0.26 Kay units⁷). The average value in the remaining 25 cases† was

*The details of this study have been reported by Ingalls.⁶

†The results of 18 cases in this series have been published in detail by Schwachman.⁸

or all of the following signs Park's so-called "corner sign," cortical atrophy, ground-glass atrophy of the ends of the shaft, Fraenkel's so-called "white line" and in many cases evidence of swelling of the soft tissues of the lower extremities

The incidence in males and females was approximately the same (Fig 1)

The seasonal distribution is rather irregular in scurvy It is sometimes said to be most frequent in winter and spring¹ Park² observed that the greatest number of cases occur in September and October

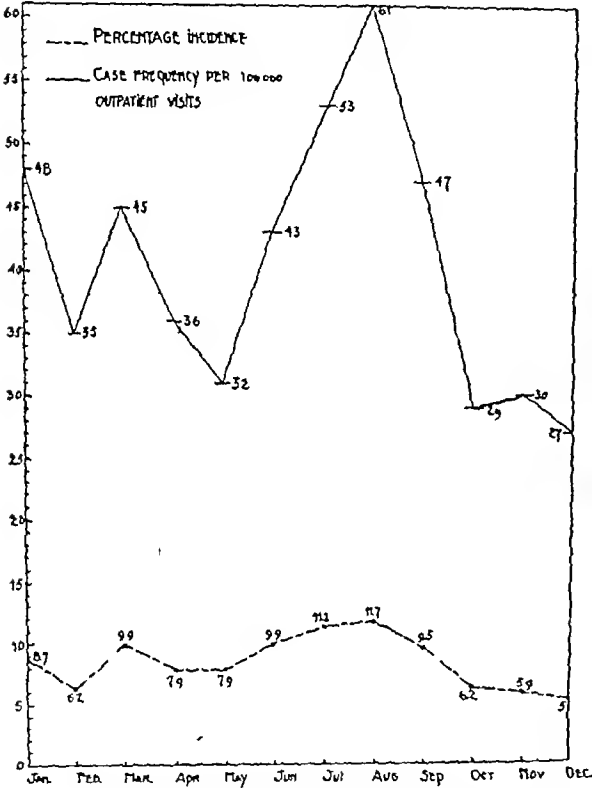


FIGURE 2 Seasonal Incidence of Appearance of the First Symptom of Scurvy (241 cases)

In the present series the incidence was high during the summer months and low in October, November and December (Fig 2)

From Figure 3 it is clear that in the majority of the cases the first symptoms appear between the ages of five and eleven months

SYMPTOMS AND SIGNS

The earliest symptoms noted are arranged in Table 1. Tenderness of the extremities was by far the most frequent complaint, and the lower extremities were affected thirty-nine times as frequently as the upper. In 15 patients the tenderness had allegedly followed some minor trauma. In 6 cases scurvy was discovered in the course of a

routine physical examination in the hospital, and in 1 case the typical roentgen-ray finding was the first noted sign, it was discovered when the patient

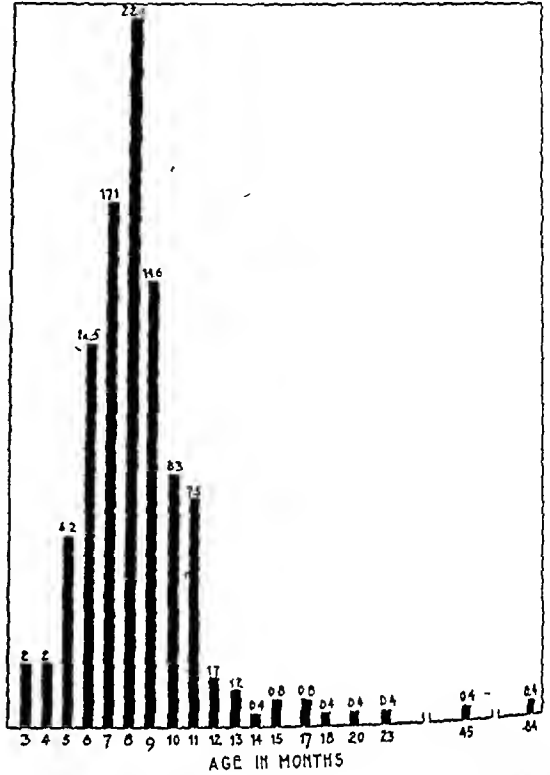


FIGURE 3 Age Distribution at the Onset of the First Symptom of Scurvy (241 cases)

The columns represent the percentage incidence in each month of age

was referred to the Department of Roentgenology for some other complaint

The principal physical findings attributable to scurvy noted at the time of the first examination are

TABLE 1 The First Symptom or Sign (241 cases)*

Symptom or Sign	No. of Cases	Percentage
Tenderness in one or both lower or upper extremities	161	67
Irritability and generalized tenderness†	59	24
Anorexia and failure to gain weight	22	9
Diarrhea or vomiting or both	15	6
Involvement of gums	15	6
Skin rash	3	1
Blood in stool	2	—
Blood in urine	1	—
No specific complaint (scurvy discovered in hospital)	7	3

*In several cases the history contained more than one early symptom, the most frequent combination being irritability and tenderness of one or both lower extremities. This accounts for the fact that the total number of first symptoms exceeds the total number of patients.

†Irritability was present in the history of 107 patients (44 per cent), but it was the earliest symptom in only 59 cases.

listed in Table 2. Tenderness in the lower extremities was eleven times more frequent than that in the upper, and swollen lower limbs were observed five times as frequently as swollen upper limbs. Gross

28 per cent, ascorbic acid in 66 per cent and both in 6 per cent

* * *

In view of the increasing efforts toward the provision for better health and the supposedly widespread dissemination of nutritional information among present-day mothers, it is surprising that one hospital should have received such a large number of definite cases of scurvy in the last ten years. The incidence in this decade was 41 cases of scurvy per 100,000 outpatient visits, as compared with an incidence of 58 cases during the previous decade. Figure 1 illustrates the steady decrease until 1940, following which a rise occurred during the next five years. The shortage of citrus fruits and their higher cost during the war years may account for this rise. The relative unavailability of physicians during the war years may have been an additional factor.

There is little doubt that mothers of scorbutic children are familiar with the idea of the necessity of vitamin C in the children's diets. The demonstrated frequency of this preventable disease, however, indicates that far more emphasis must be laid on this point in the community. Special stress should be put on the danger of the false sense of security that exists during the rather long latent period between beginning of the deficiency in diet and the onset of symptoms. The following measures are suggested in an attempt to reduce or abolish scurvy in modern communities. First, mothers

should be educated by obstetricians and pediatricians concerning the vital need of regular administration of vitamin C in adequate amounts to infants. Second, every physician should question the mother routinely concerning vitamin C intake whenever a child is seen. It is of interest in this regard that extremely few of the babies in this series had not been seen by a physician for some reason before the onset of symptoms. Hence, the fact that the intake of vitamin C was inadequate could have been determined and measures could have been taken to correct the deficiency. Lastly, the public should be educated to accept the cheaper ascorbic acid as a substitute for citrus fruits, whenever the use of the latter is not feasible.

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3.6 Bodansky units, with a range of 1.1 to 5.8 units, as compared with the mean value for normal infants of 7.2 units and a range of 4.5 to 12.0 units, as determined by Talbot and his associates.⁹

FACTORS LEADING TO AN INADEQUATE VITAMIN C INTAKE

Some explanation of the reasons for inadequate intake of ascorbic acid was given in the records of

In still another case, a physician had allegedly remarked that the canned foods for babies contained enough ascorbic acid and that additional vitamin C was not necessary. In many cases, the mother claimed that she had been faithfully offering the infant sufficient amounts of orange juice, but further inquiry revealed that in most of them the infant constantly refused it. In 7 cases, however, the informant continued to insist that the child had been

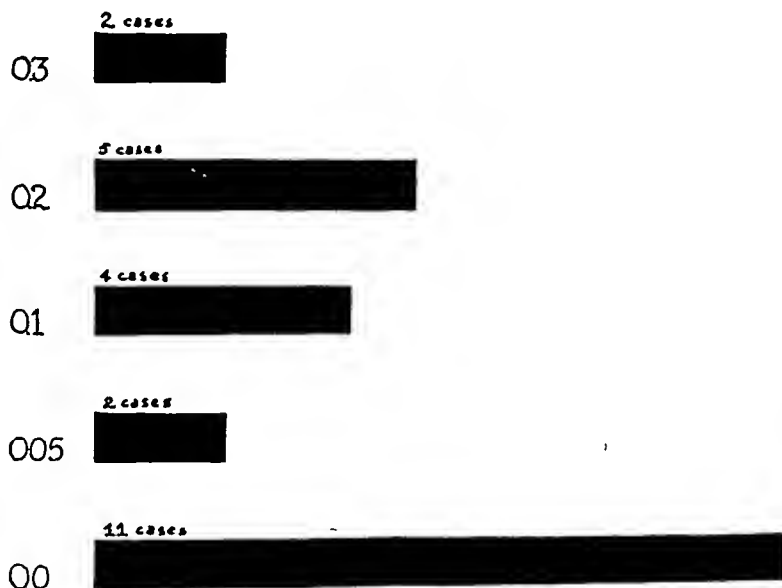


FIGURE 4 Plasma Vitamin C Levels in Scurvy (24 cases)
The figures represent milligrams of ascorbic acid per 100 cc of plasma

172 cases (Table 3). In 51 cases, orange juice was omitted because of a rash or gastrointestinal disturbances believed to be ascribable to it, without substituting vitamin C in some other form. In 28

receiving adequate quantities of orange juice or ascorbic acid.

All these cases revealed roentgenologic findings characteristic of scurvy. In all, the daily administration of 150 to 200 mg. of ascorbic acid rapidly relieved the patients of their symptoms. The alleged vitamin C intake is summarized in Table 4.

TABLE 3 Factors Leading to Vitamin C Deficiency (172 cases)

FACTOR	No OF CASES	PERCENTAGE
Baby refused orange juice	49	28.4
Orange juice caused gastrointestinal disturbances	37	21.5
Orange juice was boiled or heated or mixed with hot or boiling water	28	16.3
Too small amounts of orange juice were given	28	16.3
irregularly	14	8.1
Orange juice caused skin rash	7	4.0
Orange juice unnecessary because "adequate amounts" of vitamin C were given	2	1.2
Orange juice unnecessary because baby "getting enough sunshine"	2	1.2
Orange juice unnecessary because canned tomato juice was given daily in "adequate quantities"	2	1.2
Orange juice unnecessary because older siblings had done well without fruit juices	2	1.2
Orange juice unnecessary because "canned baby foods contain vitamin C"	1	0.6
Oranges were too expensive		
Total	172	

EFFECT OF TREATMENT

The effect of treatment was recorded in 124 cases. Most of the remaining patients were referred to

TABLE 4 Data Concerning 7 Patients Who Were Allegedly Receiving Sufficient Quantities of Vitamin C

AGE mo	VITAMIN C INTAKE ACCORDING TO HISTORY
8	2 oz. of orange juice daily, not boiled
6	3 oz. of fresh orange juice daily, not boiled and no soda added.
10	3 oz. of fresh orange juice daily, all retained
6	2-3 oz. of orange juice daily
11	25 mg. of ascorbic acid daily
7	3 oz. of orange juice daily
6	2 tablets of ascorbic acid daily during the previous 3 mo

cases, orange juice was boiled or heated or mixed with hot or boiling water. In 1 case, the mother claimed that administration of vitamin C was not recommended while the formula was prescribed

their own physicians after a diagnosis had been made and vitamin C therapy had been instituted. Relief of symptoms took place rapidly in all the observed cases. Orange juice was administered in

in each case being determined both by the patient's clinical condition and by a modicum of regard for his comfort, the total period of withdrawal, however, not being permitted to exceed three hospital days or to include more than a certain maximum of alcohol

The regimen may be summarized as follows. The diet is of high-calorie, high-vitamin type. Fluids are forced, with special emphasis on fruit juices. Liberal supplementary vitamin B₁ is given orally in all cases and intramuscularly or intravenously in those showing signs of vitamin B₁ deficiency — tremors, excessive sweating or any trace of confusion or disorientation — or giving a history of grossly inadequate recent dietary habits. Further medications include some form of antacid for control of gastric and systemic acidity and biters before each meal as a stimulant to appetite. Physiotherapy and hydrotherapy are included in the daily schedule, together with occupational therapy in graduated amounts. Psychotherapy is given so far as possible, although necessarily in only preliminary and superficial fashion during the actual withdrawal procedure. During the daytime hours, a mixture containing 0.67 gm of chloral hydrate and 2.0 gm of bromide compound is given as necessary for restlessness, but not oftener than once in four hours. At night, either 0.1 to 0.3 gm of pentobarbital sodium or 8 to 20 cc of paraldehyde is used as a hypnagogue. Whisky is used as the source of alcohol during the reduction period, in doses of 30 cc, not exceeding a maximum allowance of 240 cc during the first hospital day, 180 cc during the second and 120 cc during the third. In this study, the control cases were treated by the above regimen.

The cases in the insulin series differed in their treatment only in the addition of 10 units of insulin subcutaneously twenty minutes before meals two or three times daily and the fortification of the milk or fruit-juice interfeedings with 4 gm of cane sugar.

During the course of the study the subjective comfort of the patients receiving insulin was so definitely increased that it was believed that the usual supplementary sedation could be drastically reduced, and in the later patients of the series, 10 gm of bromide compound or 15 mg of phenobarbital, to a maximum of every four hours, was substituted for the mixture containing chloral hydrate and bromide compound. The significance of this will be referred to in more detail later.

In keeping with the previously mentioned policy of using gradual reduction of alcohol, no attempt was made in this series to withhold alcohol except as in line with the restrictions described heretofore. In a few cases the procedure was to stop whisky abruptly and institute subcutaneous insulin and intravenous glucose in the standard fashion. Patients with delirium tremens, confusion or other states of extreme toxicity, as well as those with

marked malnutrition, debilitation, vomiting or intercurrent infection, were likewise treated by abrupt withdrawal of alcohol and use of insulin and glucose. None of the patients who received the combined insulin-glucose therapy are included in this study, either as cases or as controls.

RESULTS

Duration of Withdrawal Period

The comparative durations of the withdrawal period in the 43 insulin-treated cases and in a control series of 564 patients who did not receive insulin were computed. Since the patient is inclined to judge the progress of his withdrawal by days much more than by hours or total amounts of alcohol and to adjust his demands in accord with this concept, comparison of length of withdrawal in terms of hospital days during which whisky was administered was considered to be the best standard of comparison between insulin cases and controls. With the same standard of computation applied to each, the durations may be compared with validity. On this basis, the cases receiving insulin received alcohol for slightly less than half the period required by the control cases, the average duration of the withdrawal periods being 10 day and 22 days, respectively.

Of equal significance are the comparative figures concerning the number of patients in the two groups who required no whisky subsequent to admission and in whom withdrawal was immediate. Forty-four per cent of the insulin patients received no alcohol whatsoever, as compared with only 14 per cent of the control group.

Ease of Withdrawal

It is obviously impossible to evaluate ease and comfort of withdrawal statistically. It was apparent, however, to both nursing and medical staffs that patients receiving insulin were on the whole more contented and co-operative, less restless and fault-finding and less insistent in their demands for alcohol than were the control patients. This, of course, is borne out by the figures given in the preceding section, since in all the cases, as previously explained, the reduction of the withdrawal period below the three-day limit was more dependent on the patient's comfort and co-operation than on dictum or compulsion. Not infrequently, patients who had formerly been deprived of alcohol without insulin commented on their greater comfort, both physically and emotionally, under the insulin treatment.

Requirement of Sedation

It was observed that with the decrease in restlessness and discomfort under insulin treatment, an appreciably less amount of supplementary sedation was required. As previously mentioned, this was

THE TONIC EFFECTS OF INSULIN IN ACUTE ALCOHOLISM*

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IN all toxic states, the prompt removal of the toxic agent must be the prime consideration in therapy, with the counteracting of its toxic effects and the restoration of impaired organs and their functions as secondary although vital factors. In the treatment of acute alcoholism, rapid elimination of alcohol is important, not only from the point of view of the patient's physical well-being but also for the psychologic implications, in getting him as quickly as possible through the difficult period in which he has not enough alcohol to render him emotionally analgesic, yet too much to permit clear intellectual functioning and satisfactory co-operation. Accordingly, the consideration of means of prompt elimination of alcohol in acute alcoholism has been the subject of much investigation. Attention has focused on the roles of insulin and of glucose, both singly and in combination, on the rate of alcohol oxidation and detoxification.

Chronologically, the consideration of the effects of glucose on the oxidation and detoxification of alcohol preceded that of those of insulin. The difference in effect of alcohol when taken on a full or on an empty stomach has been known to the laity for many years. It was at first assumed that the ingestion of food previous to or simultaneously with that of alcohol reduced the effect of the latter by slowing its absorption. Investigation has shown, however, that the effect is a much more specific one. Thus, Mellanby¹ and later Southgate² and others showed that food taken with alcohol reduces the level of blood alcohol, in line with this it was demonstrated that the toxicity of alcohol is in inverse ratio to the blood sugar level.³ These observations were confirmed and explained by studies showing that glucose speeds the oxidation of alcohol both *in vitro*⁴ and *in vivo*.^{5,6}

With the established intimate relation of insulin to glucose metabolism, it was inevitable that attention should also be given to the effect of insulin on the oxidation and detoxification of alcohol. Results of these studies have shown considerable variance through a voluminous literature, an excellent bibliography of which is given by Clark, Morrissey, Fazekas and Welch.⁷ The evidence for the efficacy of insulin, however, is too great to be ignored, and the preponderance of evidence has been on the positive side.^{7,8}

Clinically, the tendency has been to use insulin and glucose in combination in speeding the elimina-

tion of alcohol. The beneficial clinical results of this form of medication have been incontrovertibly established. This technic was naturally first applied in cases of pathologic intoxication and other acute alcohol toxicities such as delirium tremens and alcoholic hallucinosis. At present it is established as the recognized treatment for this group of disorders.⁹ It has, also quite naturally, been extended to use in the milder, relatively uncomplicated cases of acute alcoholic intoxication, in which it has again shown excellent clinical results.¹⁰

In all this use, the insulin has usually been considered as a secondary factor that acts indirectly by furthering the metabolism of the glucose, which is primarily responsible for the more rapid oxidation of the alcohol, so that, as has been said, "the alcohol burns in the flame of carbohydrate," much as does fat in the treatment of diabetes mellitus. Thus, in the treatment of the more grossly toxic alcoholic states, glucose is given intravenously soon after the insulin, and supplementary carbohydrate by mouth is given subsequently. The same procedure has been used in the simpler states of alcoholic intoxications. Wortis, Bowman and Goldfarb¹⁰ and others, however, have used oral glucose alone in these cases, with equally good results. It has been emphasized, however, that liberal covering of the insulin by glucose is essential and that insulin reactions must be carefully watched for.

It is the purpose of this paper to present the findings in a series of patients with uncomplicated alcoholic intoxication who were treated by being given small doses of insulin, but who were not given the usual coincident liberal amounts of glucose as such.

MATERIAL

The material consisted of 43 patients admitted for acute alcoholic intoxication, of whom 29 were men and 14 women. The duration of the acute alcoholic episode varied from two days to three months. The cases were taken at random and unselected from the group of regular admissions. It may be mentioned that, in comparison with alcoholic patients as a group, all our patients, both those included in this study and those in the control group, were in general in the higher economic and social levels.

METHOD

For some time the customary withdrawal procedure for uncomplicated cases of acute alcoholic intoxication in this hospital has been one of gradual reduction of alcohol, the actual rate of withdrawal

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†Presented before the Boston Society of Psychiatry and Neurology, Boston, November 29, 1945.

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also indirectly with the metabolism of proteins and fats, particularly the latter^{6 13} Thus, re-establishment of normal glucose metabolism also reduces the toxic effects of the intermediate metabolic products of these classes of foodstuffs

SUMMARY AND CONCLUSIONS

A series of 43 patients admitted for acute alcoholism were treated by gradual withdrawal of alcohol, with the addition to the control regimen of small doses (10 units) of insulin two or three times daily before meals, without coverage by glucose as such

The insulin-treated cases as compared with the control group showed the following clinical differences The average speed of the withdrawal period was twice as great Three times as many patients neither required nor demanded any whisky after admission Subjective ease and comfort during the withdrawal period were increased The requirement of supplementary sedation was greatly reduced, in some cases to zero The weight gain was increased by threefold, both during the first week of hospitalization and subsequently

Insulin reactions were rare and mild, being readily controlled by oral sugar

The coverage of clinically effective doses of insulin by glucose as such is apparently not a vital clinical necessity

The use of insulin in small doses deserves serious consideration in the treatment of acute alcoholism

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MEDICAL PROGRESS

DISEASES OF THE VEINS (Concluded)

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Anticoagulant Treatment

The anticoagulants, represented by heparin and dicumarol, have been extensively used in many large clinics, particularly by way of postoperative prophylaxis against thrombosis and embolism The most significant recent figures come from Swedish sources and from the Circulatory Division of the Mayo Clinic

As a background for the latest Swedish figures, the second report of Crafoord²⁸ from Stockholm may be recalled Heparin was given prophylactically in surgical cases The earlier method of continuous intravenous drip had been abandoned The drug was given routinely in four intravenous doses of something like 75 mg three times during the day, and in a dose of 125 mg to carry the patient through the night A series of 325 postoperative cases, in all of which the patients were over forty years of age, was compared with 302 control cases, not heparinized Among the latter were 33 cases of thrombosis and

embolism (11 per cent) Among the heparinized patients no thrombosis or embolism was observed, but there were 3 cases of unexplained fever, suggestive of thrombosis Outside these series, 40 cases of established thrombosis were treated by heparin, usually with excellent results, but 1 patient actually developed thrombosis and fatal embolism under heparin and died

Bauer has used a closely similar system of heparin administration, although only for recognized thrombosis The account of his²⁹ observations at the Manestad Hospital, covering the five-year period from October, 1940, to October, 1945, is illuminating No prophylactic treatment was used, but the staff watched for the earliest local and general signs of thrombosis in the lower leg, believing that 95 per cent of all such processes start in the deep (fibular) veins of the calf Suggestive signs called for phlebography If this was negative, no action was taken If it was positive, 150 mg of heparin was given intravenously and one or two more doses of the same size were given on the same day at intervals of four

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observed during the course of the study, and the amount of sedative was drastically decreased and in several cases was reduced to zero. The patients treated with a minimum of sedation or none at all did fully as well, however, as did those given the larger amounts. Thus the average period of whisky requirement was 0.9 day in the former and 1.1 days in the latter, whereas it was 2.2 days in the controls. In other words, the speed of withdrawal in both groups was essentially twice that of the controls.

Nutrition and Weight

The comparative average gain in weight during successive weeks of hospitalization was calculated for the 43 insulin-treated cases and for 40 control cases. During the first week, which included the actual withdrawal period, patients treated with insulin gained on an average of 2.0 pounds, as compared with 0.6 pound in the controls. During the second week, the average gains in weight were 1.9 pounds in the insulin cases and 0.5 pound in the controls. During the third week, the average weight gains were 1.1 pounds and 0.4 pound, respectively. Both the insulin-treated patients and the controls were served the same diet, although no patients were forcibly fed on the one hand or refused second servings on the other.

Circulatory Changes

Recordings were made of blood pressures and pulse rates as readily determinable indications of circulatory function. The findings in regard to blood pressure showed no consistent trends. Thus, approximately equal portions of the two groups showed a rise of blood pressure above the admission level by the end of the first week of hospitalization, a fall below the admission level and no appreciable change in blood pressure — that is, difference of less than 5 mm diastolic and 10 mm systolic. In general the changes, when they were appreciable, showed approach toward more normal levels. Pulses were characteristically found to be rapid, full and bounding on admission, with a later fall in rate and improvement in quality.

There was no appreciable difference in the two groups.

Insulin Reactions

Among the 43 cases, there were only 3 cases of insulin reaction at a clinical level. Two of these occurred within one hour of the insulin injection, and the third occurred after a lapse of four hours. All the reactions were extremely mild, being characterized by slight perspiration and a feeling of weakness, without changes in pulse rate or blood pressure. They were readily controlled by the administration of 250 cc of orange juice fortified with 20 gm of cane sugar. In no case was it necessary to have recourse to intravenous glucose, which, however, was always available.

COMMENT

The findings described above are of significance not only as demonstrating clinically the effectiveness of the administration of insulin without glucose but also as perhaps shedding some further light on the whole matter of the relation of insulin and glucose to alcohol oxidation. Interpretation of these findings may take one of two main lines.

On the one hand, it may be assumed that the good clinical results are due not to any direct effect of insulin but rather to the effect of glucose already present in the body or derived from the subsequent meal but mobilized by the insulin given. To be sure, the dosage of insulin in this series was relatively small (10 units) and could be covered without too much difficulty by the glucose deriving from the carbohydrate of the subsequent meal. Yet the clinical results demonstrate that whatever amount of insulin was given was of significance. At the same time, the infrequency and mildness of insulin reactions in these cases indicate that the amount of glucose available must be not inconsiderable. Of course, there are the glycogen stores of the liver and muscles, but these are likely to be more or less depleted in the alcoholic patient, and one would hesitate to deplete them further. It appears, however, that dipping into these stores may not be essential to cover any deficit in the food. It has been observed that alcoholic patients show reduced sugar tolerance and high blood-sugar curves, with ready propensity to hyperglycemia and glycosuria.¹¹ This may be due to the fact that when alcohol and glucose are simultaneously present in the blood, the alcohol tends to be oxidized in preference to glucose.¹² Furthermore, with the usual deficiency of carbohydrate in the diet of the average alcoholic patient, there is a lessening of the usual stimulus for endogenous insulin production, so that for this reason also glucose oxidation is impaired. By the administration of insulin, therefore, as in this series, the metabolism of this otherwise impotent glucose is furthered, and there is a breaking up of the vicious circle in which alcohol directly or indirectly interferes with the metabolism of the element — that is, glucose — that would in turn otherwise speed the elimination of the alcohol itself.

On the other hand, Clark, Morrissey, Fazekas and Welch⁷ have shown by experimentation with animal tissues both *in vitro* and *in vivo* that in the initial oxidation of alcohol by the liver insulin is in itself an essential factor, apart from glucose. Accordingly, the administration of insulin alone, as in this series, would be of direct significance in the oxidation of the alcohol present without necessarily being entirely dependent on glucose metabolism.

In considering the clinical picture of acute alcoholism and the clinical results of insulin treatment, it must also be borne in mind that alcohol interferes not only with the metabolism of carbohydrate but

tolerance test and the thromboembolic problem in general

Thrombosis following leg injuries has been serious enough to call for special treatment by both operative and chemical methods. Allen Linton and Donaldson⁷ speak briefly of prophylactic vein ligation in fractures of the hip. Golodner, Morse and Anguist⁸ found that among 86 fatalities in 504 cases of fractured hip 25 autopsies revealed 9 cases of pulmonary embolism. There may, of course, have been many more, but in any case pulmonary embolism was the most frequent cause of death. These authors recommend prophylactic, bilateral superficial femoral-vein ligation combined with sympathetic lumbar block, especially for patients who cannot be made ambulant early.

Bauer⁹ finds the incidence of thrombosis in leg injuries to be 12 per cent, as compared with 1.6 per cent after surgical operations, 10 per cent after childbirth and 2.1 per cent in medical patients. It occurred almost exclusively in the injured leg. He believes that many cases have gone undiagnosed or at least have not been diagnosed until persistent swelling and pain have called attention to the late stage of the process. Since diagnosis is particularly difficult in the case of fracture, because of plaster casts, splints and other apparatus, he recommends, besides the usual elevation of the foot of the bed and the greatest possible use of the muscles, the routine administration of heparin in the same dosage as in the postoperative group of cases. Under this treatment, he finds a reduction in the mortality from pulmonary embolism in traumatized patients, during three years of trial, to less than one fifth of that previously observed.

Complications of Thrombosis

Bauer's⁹ exhaustive monograph on the sequelae of thrombosis deserves detailed study. It is written with the point in mind that since 97 per cent of all obstructive femoral thromboses start in the lower leg, it is most important that early diagnosis be made and that efficient treatment (by heparin) be given to prevent the process from reaching even the popliteal vein. For once an obstructive thrombophlebitis — phlegmasia alba dolens — has become established one must expect that edema of some degree will follow in 100 per cent of the cases. Moreover, indurations, such as often lead to ulcers, are present in 45 per cent at the end of five years, in 72 per cent at the end of ten years and in 91 per cent after a still longer period. Bauer holds that a deficient venous return is always responsible for the edema, and he ignores both lymphatic and vasoconstrictive elements in the edema problem. One must admit the significance of Bauer's figures without fully agreeing with his explanation of postphlebotic edema and induration.

I myself have been interested for years in the postphlebotic leg and have regarded edema as the

basic change that leads to so much misery and incapacitation. In a paper read before the New England Surgical Society in 1946 and now in process of publication I presented an account of the various late complications as I had encountered them in ambulatory patients outside a hospital clinic (Hospital practice includes an unduly high incidence of ulceration). Edema was very frequent, induration and ulceration were second in importance and there were also found many cases of a mild causalgia-like pain complex of recurrent thrombosis and of venous congestion including varicosities. It did not seem to me that venous stasis was the whole story. There were late effects resulting from the intense peripheral vasoconstrictions of the acute disease, which could be relieved by sympathetic lumbar block or sympathectomy and there were cases in which there was present not only a secondary saphenous varicosity but what might be called femoral varicosity as well.

I¹⁰ had previously presented the view that in some postphlebotic states the recanalized femoral vein might be regarded as the source of stasis and back pressure or even back flow of venous blood. In selected cases the femoral vein might be sectioned with satisfactory results, the leg being afterward less heavy and congested. The explanation seemed to be that since the femoral vein was functionally useless a collateral circulation must necessarily have been established and treatment of the femoral as a varicose vein was therefore entirely logical. In a limited series, these conclusions have proved to be correct, although I cannot see that edema has been favorably influenced by the operation. In some cases I have interrupted the vein at a level higher than the inguinal ligament.

Buxton and Coller,¹¹ who have taken a similar view, make their second report of postphlebotic femoral-vein ligation. Superficial varices have been sectioned along with the deep veins (femoral or common iliac). Ulcers have as a rule been cured, although the authors are not convinced that the good care given their patients has not contributed more than the operation to the favorable result in some cases. Operations done mainly for edema and fatigue have been disappointing.

My comment is that the postphlebotic state deserves more study than it has hitherto received. Possibly as Bauer suggests early restraint of thrombosis by anticoagulants will prevent many of the present-day complications. Once the femoral vein is fully obstructed, surgical attack with thrombectomy may act much like lumbar sympathetic block in doing away with reflex vasoconstriction and its consequences. Should the anticoagulants prove fully as life-saving as operative measures or actually more so, they will probably be preferred as securing a better postphlebotic leg. For in early cases, at least they should leave behind a functioning valved upper and perhaps even lower femoral vein.

hours. Then, three daily doses of 100 to 150 mg each were administered, without any study of the blood. In four or five days the temperature usually returned to normal, local signs in the leg disappeared, and the patient was made ambulatory, after one more day, heparin was withdrawn. The average stay in bed was 4.7 days, and the average total dose of heparin was 1700 mg.

In 209 cases of proved thrombosis so treated there were 3 deaths from embolism, all nonpostoperative, a mortality of 1.4 per cent, as compared with 18 per cent in earlier (control) years. Since heparin was not given until five to seven days after operation, no hemorrhage of consequence occurred. Special advantages of this line of treatment were found to be a greatly shortened convalescence and such a restriction of the thrombotic process that the secondary complications of edema and venous congestion were almost completely absent. The confinement of thrombosis to the lower leg and preservation of the popliteal vein were looked on as decided gains resulting from the treatment, but if phlegmasia alba dolens had developed, the use of heparin, although seemingly effective, did not ward off the late secondary complications.

It will be noted that Bauer does not claim 100 per cent success from this system and makes it clear that its use calls for early and accurate diagnosis. For those who wish to study Bauer's method in detail, his exhaustive paper on the sequels of thrombosis⁹ and his account of thrombosis following leg injuries¹⁰ are also available.

Barker, Cromer, Hurn and Waugh³¹ have published a report on the use of dicumarol in the prevention of postoperative thrombosis and embolism, based on 1000 cases at the Mayo Clinic. They make a special point of dosage and safe administration. The drug was given routinely, and the prothrombin deficiency was estimated by daily blood tests after the method of Quick. They tried for a prothrombin time of thirty-five seconds (bleeding did not occur if the time was under sixty seconds), which corresponds to 20 per cent of prothrombin in the blood plasma. No fatal pulmonary embolism occurred during the one to three days between the first administration and the establishment of the required prothrombin deficiency. Dicumarol was preceded by temporary administration of heparin and the prothrombin deficiency was maintained for several days to a week after the patients had become ambulatory. Actually, the deficiency might continue for two to ten days after administration had ceased, so that daily tests were kept up until normal levels were reached.

Some patients, most of whom had suffered no thrombosis or embolism, were found to be highly sensitive to dicumarol. In such cases the prothrombin level might fall to less than 10 per cent after the first one or two doses. Bleeding was likeliest to occur in this group and required control

by blood transfusion and large intravenous doses of menadione bisulfite (synthetic vitamin K). The doses of dicumarol used were, it seems to me, rather large — 300 mg on the first day, 200 mg on the second day and 200 mg on each succeeding day that the prothrombin in the blood was more than 20 per cent of normal.

The authors hold that even when a thrombus is present, dicumarol will prevent embolism, since old thrombi remain attached to the walls of the veins, and they regard it as the treatment of choice for serious embolism when its source is obscure.

Another instructive account of dicumarol administration comes from Reich, Hahr, Eggers and Lipkin.³² Both prophylactic treatment (102 surgical cases) and treatment of established thrombosis (33 cases) and embolism (9 cases) were employed. These cases arose among 2591 surgical and obstetric experiences. Uniformly favorable results were secured, and no fatalities resulted. The authors question whether routine use of dicumarol is advisable but are convinced that the drug should be given in all cases in which thrombotic complications are likely to arise, including pelvic operations, intra-abdominal cancer and surgical procedures in patients who have shown a previous tendency to thrombosis. Heparin may properly be given, it is stated, during the latent period before dicumarol produces its effect. Tables of dosage are offered.

In choosing an anticoagulant, one should have in mind the promising method of administering heparin devised by Loewe and his associates.³³ These authors have taken up the Pitkin menstruum, a gelatin-dextrose-acetic acid combination, as a means of delivering heparin to the patient over a prolonged period. They have worked out the required dosage and the appropriate intervals, with and without the aid of vasoconstricting drugs. According to their latest report they had treated 125 cases of thromboembolic disease, 42 of which had already suffered pulmonary embolism. Among these 42 cases were 4 fatalities, which are reported in detail. Clinical improvement, as a rule, was striking. Heparinization, these authors believe, must be continued for ten to fourteen days in uncomplicated phlebothrombosis, but when pulmonary infarction has occurred three or four weeks are required. The full heparin effect must still be present when the patient is first allowed out of bed. Lange and Loewe³⁴ record further experience with the method in the treatment of experimental human frostbite. It should be noted that earlier trials with the intramuscular injection of heparin itself, as attempted by Walker,³⁵ had proved that such injections were very painful. Walker also used various menstruums.

De Takats and Fowler,²¹ who have previously been quoted as making use of both operative and chemical methods, give an excellent account of the combined heparin-dicumarol sequence, their heparin-

of cases, he has encountered a minimum of accidents, and reports excellent results

For Sherman's method of injection and stripping, a system of stripping with actual exposure and section of the large branches as they join the varicose saphenous vein in the thigh might well be substituted — a procedure long used by me in former times and recently advocated by Sapiro⁴⁶ It is probable, however, that Sherman's retrograde injection does not offer the same hazard of penetration of strong solutions through direct perforating veins into the deep system, as is incurred when retrograde catheterization and injection down into the veins of the lower leg are employed Lyall⁴⁷ strongly recommends this retrograde injection (after Pratt's plan) although he notes some disturbing post-operative febrile reactions of considerable severity (One may well ask whether some of these reactions are not evidence of a deep thrombophlebitis) Smyth,⁴⁸ who also uses Pratt's retrograde catheterization into the veins of the calf again notes a number of complications, including reactions to the sclerosing agents My own comment on these observations is to question the value of such retrograde injection Probably it ensures a little more thorough severance of all possible varicose connections, but considering its occasional undesirable effects and its failure to obliterate permanently the veins it enters (mere thrombosis does not mean obliteration), I question the advisability of its continued use

It is worthy of note that McPheeters,⁴⁹ the exponent par excellence of the injection treatment of varicose veins, writes in favor of saphenofemoral ligation with immediate retrograde injection, stating that "the theory that the preliminary ligation is the first and perhaps the most essential step in the treatment is based on the now proved fact that the flow of blood in any well developed cases of varicose veins is actually reversed" — a matter that he had a large part in demonstrating He advocates emptying the leg veins by elevating the foot of the table during the operation and, on reversing this position, injecting two thirds of the sclerosing solution into the lower saphenous stump Thus, he believes that he fills all saphenous tributaries down to the foot As complications, he cites occasional severe chemical phlebitis and the associated cellulitis following the injections of too large amounts of the sclerosing solution He has seen cases in which the lower leg and even the thigh were swollen after operation

For an account of a return nearly to the radical dissections of earlier days one should read Hodge, Grimson and Schiebel's⁵⁰ paper on the treatment of varicose veins by stripping, excision and evulsion A review of the older surgery is given The authors treated many difficult cases, including postphlebotic varices and those complicated by ulcer They carried out the usual full dissection in the groin and then removed the varicose veins by stripping and

evulsion down to the ankle, making some lower-leg dissections and undercuttings They applied pressure bandages and used early mobilization In a fairly short series (195 cases) they encountered no pulmonary embolism

I have tried here to show how the treatment of varicose veins has swung more than a full circle Actually, it has gone from injection to Trendelenburg's ligations in the thigh, to radical dissection, including that of the lower leg, then back to injection again, to high ligation plus injection and now to radical dissection The conscientious surgeon should recognize these cycles and draw conclusions accordingly

A freakish sort of varicosity is described by Prioleau⁵¹ as originating from the gluteal vein Such a congenital anomaly is not difficult to identify, but it recalls the hemangiomas, which closely imitate saphenous varicosity The importance of these lesions lies in the danger of dealing with them surgically Immediate and late hemorrhage are serious dangers

The value of venography in the diagnosis and treatment of varicose veins is discussed by Imler, Beaver, and Sheehan⁵² Because they regard varicose veins associated with deep venous obstruction as compensatory, they believe that clinical tests should be supplemented by venography in case the state of the deep circulation is uncertain Should the deep veins be found obstructed, recurrence after operation for varicose vein must, they say, be expected Thus, a knowledge of the state of the deep circulation may warn against operation My comment is that varicose veins do not forward venous blood against gravity Therefore, a collateral circulation by nonvaricose veins must have been established after a deep thrombophlebitis, if the lower leg is not observed to be grossly congested and cyanotic If this is true, — and it seems unassailable to me, — obliteration of varicose veins must always be of benefit, regardless of the state of the deep circulation, and need not result in recurrence Phlebography, however, should give a more complete picture of varicosity in complicated cases than routine tests and should permit a more accurate operation

Arterial spasm, secondary to ligation and retrograde injection of varicose veins is discussed by Tunick, Nach and Weinkle⁵³ These writers studied the resulting arterial constrictions by oscillometry in 50 cases of saphenous varicosity so treated They agree with DeBailey, Burch and Ochsner's⁵⁴ earlier observation that irritation of a venous segment causes reflex arterial spasm This spasm corresponds in degree to the violence of the local reaction Clearly it may be very dangerous, in the presence of states of arterial deficiency, and it perhaps accounts for some of the cases of gangrene of a leg that rarely result from varicose-vein operations

As a final word on the thromboembolic problem, I quote parts of two recent editorials, which should of course be read in toto Allen³⁹ writes

Due to the immensity of the problem in the Massachusetts General Hospital, there has come about a gradual but steady trend toward femoral-vein interruption as an answer to this question. To August 1, 1945, 861 patients in this institution have been subjected to femoral-vein interruption. At first, attempts were made to determine whether or not a thrombus existed, by phlebography — now this method has been abandoned. Early, we learned that the apparent sick leg might be misleading and that often the most dangerous thrombosis was lying dormant in the opposite, apparently normal, side. Therefore, we have gradually become convinced that bilateral interruption should be done.

In this series, there has been no fatality as a result of the procedure. There have been surprisingly few instances of infection or lymphorrhea. Only one of the patients has developed a postphlebotic ulcer. The average hospital stay after femoral-vein interruption has been about six days. Patients operated upon before leg swelling develops have no postoperative edema worthy of note. If the operation is undertaken after bland thrombosis has become inflammatory with pain and swelling, then a period of postoperative edema occurs.

This operation is so safe and so simple and if done on the normal vein produces so little swelling of the extremity, that prophylactic vein interruptions are being done with greater frequency. Up to the date of this writing, this procedure has been carried out in approximately 100 patients in our clinic. All of this group have been elderly patients, who, for reason of their acute disorders, would need a prolonged period of bed rest. Typical of these are the aged with fractures of the hip region.

Allen goes on to allude to the tentative use of dicumarol in his clinic by which fewer operative interruptions may be needed. Collier⁴⁰ writes

The formation and propagation of thrombi in the vascular tree must be prevented by promoting normal physiologic processes, if the process is initiated it must be stopped. The measures used by the surgeon must be simple, readily available and effective. The treatment of thromboembolism as a complication must neither affect adversely the primary disease nor interfere nor complicate the treatment which is essential to this disease. The morbidity and mortality associated with the accepted therapy must be minimal. When these criteria are fulfilled, the problem of thromboembolism will no longer be a problem.

OBSTRUCTION AND THROMBOSIS IN VARIOUS VEINS OF THE BODY

Primary thrombosis of the axillary vein is discussed by Roelsen,⁴¹ who has observed 7 verified cases. He describes the usual swelling, heaviness and congestion of the arm, associated with dilated veins about the shoulder. Apparently these same signs may develop in the absence of actual thrombosis, for obscure reasons. Roelsen finds heparin useful in the acute stages of axillary thrombosis, is opposed to operative interference (resection) except in chronic or recurring disease and advises against immobilization of the arm.

The superior vena caval syndrome is exhaustively described by Hussey, Katz and Yater.⁴² Obstruction of the superior vena cava has received renewed attention since phlebography and measurements of venous pressure have become available. The disorder is usually secondary to thoracic tumors and to aortic

aneurysm, but may also result from the establishment of a fistula between an aneurysm and the great vein. The symptomatology, according to these authors, is related not only to the caval obstruction itself but to the underlying disease as well. Thus, dilated veins on the neck, chest and arms are frequent, and edema is often present in this same field. Dyspnea and cyanosis could equally well be related to the venous obstruction and to the intrathoracic growth or aneurysm. The authors describe methods of measuring venous pressure and present many striking phlebograms. They call attention to improvement that may result from the irradiation of radiosensitive growths and to the occasional value of surgical exploration.

Elective occlusion and excision of the portal vein is discussed by Brunschwig, Bigelow and Nichols.⁴³ The matter came up, in their experience, because of injury to the portal vein in the resection of a malignant pancreatic tumor. Finding, in an autopsy on their patient, that gradual occlusion of the mesenteric veins had resulted in many anastomoses with the vena cava, they undertook experimental occlusion of the portal vein in laboratory animals. Omentopexy was found to be useless, but if the portal vein was gradually severed by a loop of linen thread, subsequent resection of the vein was compatible with normal life in 2 of their 4 animals.

VARICOSE VEINS

In my last review, I¹ called attention to publications recognizing the significance of anatomic relations and venous pressures in the etiology and treatment of varicose veins. Possible dangers in the retrograde injection of sclerosing solutions were also considered. Since then, a swing toward increasingly radical operations has become plainly evident, and local anatomic variations in the groin and thigh have again been emphasized.

A thorough study of the saphenous vein and its tributaries near its entrance into the common femoral vein, based on anatomical dissections in 550 cases, is offered by Daseler, Anson, Reimann and Beaton.⁴⁴ A great variety of patterns are pictured. With such information in mind, a surgeon can have no excuse for not thoroughly eradicating all connections between the varicose saphenous system and the valveless deep veins in the region of the inguinal ligament and above. I am never tired of pointing out that this, of course, is the chief consideration in the successful treatment of varicose veins.

Sherman's⁴⁵ anatomical studies of the connections of the superficial with the deep veins of the thigh have led him to perform a stripping operation, under a general anesthetic, combining this with retrograde injection of a sclerosing solution into the lower saphenous stump, to control the bleeding that might otherwise result from the rather rough eradication of so many saphenous branches. Employing early ambulation, in a considerable series

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 32321

PRESENTATION OF CASE

A twenty-eight-year-old bipara entered the hospital complaining of pain in the lower abdomen.

About two years before admission attacks of moderately severe, steady, aching, nonradiating, bilateral, lower abdominal pain began, occurring two or three days before each menstrual period and lasting until the end of the flow. Occasional sharp stabbing pains were also noted. Similar episodes of dull aching and sharp twinges in both lower quadrants, varying greatly in intensity and duration, were present intermittently throughout the month. Concomitantly the periods, which had previously occurred regularly every twenty-eight days, became irregular, and the flow became variable, lasting three to seven days. The patient passed many clots and sometimes had cramps at the time of passage. Her condition gradually increased in severity, and during the few months before admission she had lost 18 pounds. Her last menstrual period occurred seven days before admission.

The patient had been healthy except for two attacks of pneumonia in childhood. Catamenia had begun at the age of thirteen years and had always been regular until the present illness, although she had had cramps during the first day or two of the period, until the birth of her first child six years before admission. After her second pregnancy, three years later, she had been told that there was a cyst in the right ovary. Both babies had been delivered at full term by forceps, the second being a breech delivery. The breasts had become slightly tender before each period.

Physical examination showed a young woman who appeared entirely normal except for an irregular pelvic mass in the lower right vault, with a ridge extending across the posterior cul-de-sac behind the upper cervix.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 80 diastolic.

The urine, blood and hemoglobin were normal, and the blood Hinton reaction and a chest x-ray film were negative.

Because of a mild upper respiratory infection, with moderate nasal discharge and a reddened throat, operation was delayed until the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD ULFELDER: This patient was a young mother with symptoms referable to a pelvic mass of several years' duration. Although the history and the physical findings increase the likelihood of one diagnosis over others, the results of the studies are not conclusive and merely suggest strong possibilities.

Several points in the history seem to bear on the problem. The patient had been in fairly good health and had had two children, three and six years old. The marital history had been uneventful until the time of the present illness, when both the duration and the interval of the periods became irregular. The history suggests that true menstrual cramps had not been noted until the onset of the present illness, when she noticed bilateral lower abdominal pain that seemed to be worse at the time of the periods. Apparently the symptoms had gradually grown severer, without any abrupt change. The loss of 18 pounds during a few months is noteworthy, but I should like to know more about the appetite and food habits before attempting to evaluate the significance of the weight loss.

Physical examination revealed an irregular mass in the right vault and posterior cul-de-sac. One would like to know whether the physical examination showed evidence of weight loss. One would also like to know the size of the mass and whether it was tender or movable, and whether the uterine fundus and cervix appeared abnormal in any way.

DR. OLIVER COPE: So far as weight loss is concerned, the patient was not conscious of any change in her food habits but realized that her appetite was impaired. She felt generally less well. The physical examination was entirely negative except for the mass in the pelvis, which could be felt behind the cervix, better by rectum than by vagina. The prominent part was more to the right side than to the left. The mass was small, plum-sized, quite hard and, apparently, adherent to the upper part of the cervix or to the lower part of the uterus. The fundus of the uterus was normal in size, was freely movable, and could be distinctly felt, because the patient was quite thin. The mass, which was principally on the right, extended over to the left with a suggestion of irregularity and of diminishing size, disappearing into the left vault. Neither ovary was identifiable, but there was apparently nothing higher up in the vault. The cervix showed minor erosions compatible with two pregnancies.

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surgical castration and closure of the incision, with subsequent castration by x-ray

DR. ULFELDER My decision in this case would have depended on my evaluation of the patient — whether she wanted more children, and how she would react to the idea of surgical castration. It would make a difference whether the possibility of castration had been discussed before operation.

DR. FRANCIS INGERSOLL I do not believe that I should have castrated the patient at the time, not knowing the entire story, because endometriosis is known to be slow in development. Many patients whose entire ovarian tissue appears destroyed by endometriosis of both ovaries have later had children with apparent ease. I remember one such patient who has had three children and is again pregnant. The lesion is not malignant and can be checked at any time with x-ray treatment. It therefore seems wise to me to leave the ovaries and see what happens in the future, the status of the disease may not change for years.

DR. BENJAMIN CASTLEMAN Did this patient show signs of obstruction of the colon?

DR. COPE No. About one third of the circumference of the sigmoid was involved. That fact entered very decidedly into the decisions in handling the case, because I believed that any extension of the disease would have caused intestinal obstruction. We had made a tentative diagnosis of endometriosis preoperatively and had discussed the possible implications with both the patient and her husband. I was also influenced by the facts that the patient had been examined by competent hands and that the disease had appeared in six months and was considered to be growing rapidly, and I believed that intestinal involvement had something to do with the weight loss. In other words, we were dealing with a rapidly progressing lesion whose major involvement was in the gastrointestinal tract. The patient had two children and desired no others. Both husband and wife were reconciled to the idea of castration if that proved necessary. We therefore decided on castration, and we resected the ovaries rather than waiting for additional information. In fact, we thought that the disease had progressed to the point of requiring castration by one method or another.

Dr. Ingersoll's point is well taken, but I was not sure that another pregnancy would occur. The patient faced a very disagreeable time whichever decision we made. I hate to castrate anybody, particularly a woman of her age. But it seemed worse to allow her to face a permanent colostomy. How soon can the patient be safely relieved of the disagreeable symptoms of the menopause by partial replacement therapy? It seems obvious that adequate replacement therapy is contraindicated because the endometriosis would be stimulated to a tumorous growth. Can enough replacement therapy

be given to help the patient through the uncomfortable period after acute menopause?

DR. ULFELDER I believe that symptoms would flare up again regardless of what was done.

DR. INGERSOLL Theoretically, the symptoms could be exacerbated by estrin, which could, however, be used for temporary improvement and control of the hot flashes.

CLINICAL DIAGNOSIS

Endometriosis

DR. ULFELDER'S DIAGNOSIS

Endometriosis

ANATOMICAL DIAGNOSIS

Endometriosis of sigmoid, rectum, bladder and left ovary

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN The material we received showed a tiny area of endometriosis on the back of the left ovary, and none on the right. The biopsy specimen that Dr. Cope took from the dome of the bladder and sigmoid also showed endometriosis. Dr. Cope's point about involvement of the sigmoid is important because resection of the sigmoid has been necessary in almost all the cases with involvement of the sigmoid that have been seen in this hospital. I do not believe that x-ray treatment would have relieved the obstruction, once the scarring had gone so far as to produce obstruction of the sigmoid. Resection of the sigmoid would have been necessary.

DR. COPE That point is worth emphasizing. We thought that the intestinal lesion was potentially malignant and that extreme measures were required from an endocrinologic point of view. The disease, of course, was not malignant, but its distribution was

CASE 32322

PRESENTATION OF CASE

A forty-five-year-old housewife entered the hospital because of postprandial pain.

About two years before admission the patient first noticed attacks of stomach pain that occurred one or two hours after eating. The pains became progressively worse, and nausea and vomiting developed. Prescribed medication and diets gave no relief. X-ray studies seven months before admission were said to have shown an ulcer. During the illness the patient had lost 45 pounds, but she had regained some weight in the last few months, apparently as the result of marked symptomatic relief obtained from a new regime of diet and medication.

Four years before admission a hysterectomy had been performed for fibroids.

DR ULFELDER Was the mass movable and nontender?

DR COPE No, it was fixed and slightly tender

DR ULFELDER Abdominal and chest films, a barium enema, an Aschheim-Zondek test and anything that might give some clue regarding the nature of the palpable mass would be helpful I believe that only a plain abdominal film and a chest film were really indicated, since surgery was imperative and the risk of operation minimal Was an abdominal film taken?

DR COPE No, it was not And a barium enema was not given because the mass seemed clearly to be in the posterior cul-de-sac We doubted whether a barium enema would show anything

DR ULFELDER That was my opinion from the history

DR COPE I also doubt whether a plain abdominal film would have shown anything An x-ray film of the chest was taken in spite of the negative physical examination, on the principle that in a patient who had lost so much weight tuberculosis should be excluded

DR ULFELDER This lesion must have been of several years' duration The change in menstrual habit strongly suggests sufficient involvement of both ovaries to interfere with normal ovulatory rhythm Three diagnoses appear possible in this case involvement of both ovaries in an ovarian tumor, endometriosis and chronic pelvic inflammatory disease Nothing in the history supports the last diagnosis The pregnancies three and six years before admission militate against, although they do not actually exclude, endometriosis The pain with the periods and the description of the mass, especially in the cul-de-sac, are points in favor of endometriosis The most probable ovarian tumor in this patient is dermoid, and dermoid is bilateral in about 20 per cent of cases Mention should also be made of unilateral ovarian tumor, with endocrinologic activity with the production of estrin Granulosa-cell tumor is the most frequent of such lesions Tuberculosis must also be excluded

My diagnosis is endometriosis, in spite of the fact that the patient had recently had children The likeliest type is endometriosis involving both ovaries and the adnexa in the usual fashion, and I base this diagnosis on the history of pain with the periods and the finding of a fixed mass in the vault extending down into the cul-de-sac

DR COPE Examination under ether revealed nothing beyond what had been observed without anesthesia We did not definitely identify the ovaries apart from the mass (I hope Dr Ulfelder will comment on these findings later) When we dilated the cervix to see what the endometrium looked like, we could easily look up into the cervix, where there were small, 2-mm long, firm, polypoid irregularities, which did not bleed easily but were a matter of concern in judgment of what was sub-

sequently done This was not the usual fleshy type of polypoid mass that eventually extrudes from the cervical canal The endometrial tissue was whitish, consistent with a postovulatory phase, and was grossly somewhat firm, as if slightly fibrosed, but was considered normal The uterine cavity was obviously normal, except for the mass that was adherent behind to the upper cervical segment The lower part of the uterus was lobulated and larger on the right, so that the mass might have been taken for a cervical fibroid, but I did not believe so On opening the abdominal cavity exploration was negative, except that the tip of the appendix was definitely bulbous, as in a carcinoid appendix—the patient had had no recent attack suggesting a subsiding inflammation The uterus was normal Both ovaries and tubes were grossly normal, except for one small area behind the left ovary, which contained a small punctate bluish cyst On the dome of the bladder on the left side was a puckered area of fibrous scarring, with retraction not more than 1 cm in diameter containing a half dozen small blue cysts This area was later excised and given to Dr Castleman That was all the disease, except for the mass in the pelvis, which proved to be the rectum and sigmoid involved in three areas of endometriosis, the upper rectum and sigmoid were puckered and attached firmly to the back of the upper part of the cervix and the lower part of the uterus From this description it can be seen that we agreed with Dr Ulfelder's diagnosis

At first excision of the three areas of endometriosis appeared possible We divided the peritoneum 0.5 cm away from the areas of gross endometriosis and began to dissect down the sigmoid in the muscular layer The first area of endometriosis on the sigmoid was resected easily enough, the second with slightly more difficulty When the rectum was reached it was clear that the third area could not be resected the disease had infiltrated so deeply into the muscular wall that it would have been necessary to resect the rectum More careful inspection of the areas of the sigmoid that had been freed showed that the disease had penetrated into the muscularis When the muscular layer of the sigmoid was opened two cysts popped out, and deep invasion was unmistakably present We did not know whether the disease extended to the mucosa itself, but it clearly went deeply into the mucosal layer, and to resect the tissue, a combined resection of the sigmoid and rectum, with a permanent colostomy, would have been necessary I should like Dr Ulfelder and others to comment on what they would have done at this stage

DR ULFELDER Such a decision is extremely difficult in a patient under thirty years of age

DR COPE The endometriosis was limited to one area on the left ovary and to one on the bladder that was resectable and localized to the rectum, sigmoid and back of the uterus The two alternatives were

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To date, the progress of the Study has been most encouraging. Throughout the country most of the state programs are being promulgated by experienced physicians who have returned from the war realizing that a new order is in the offing. Before resuming their former activities, they have been challenged by this opportunity to take inventory of one part of medical practice.

The Study may now be said to have been completely organized. Programs are under way in all the states, and regional conferences have been planned for the early fall to consider the form that national and state reports should take. Substantial funds, largely from voluntary sources, have permitted the work to be carried on with the proper perspective for a work of national proportions. In New England, substantial contributions have been made by the National Foundation for Infantile Paralysis, and in Massachusetts, by the newly formed Bay State Society for the Crippled and Handicapped. In all the New England states, the project is not only launched but well afloat. Rhode Island has practically completed its part in the survey. A pilot study, already finished in North Carolina, has clearly shown that physicians busy in practice regard this as something more than just another survey and that pediatricians consider it a serious responsibility.

The national committee is now considering how to make the best use of material from the questionnaires. In the near future, it will be possible to announce the statistical methods that will be adopted. Although it is clear that many already know deficiencies in medical care will be re-emphasized, it is expected that new light will be shed on the amount of service contributed by practitioners of medicine and dentistry, on the quality of service available in clinics and institutions and on the actual scope of present pediatric practice. All these data should form a basis for future concerted action on the part of pediatricians to improve and extend present health services to children.

Already important side lights of the Study have been observed. It is making legislators reluctant to advance new panaceas for the improvement of medical care until the questionnaires are processed. Furthermore, a great awareness of the importance

STUDY OF CHILD HEALTH SERVICES

THE medical profession has been well informed through editorials in the *Journal* and the *Journal of the American Medical Association* and through the public press of the Study of Child Health Services. It warrants reiterating that the study is being conducted not only by the members of the American Academy of Pediatrics but by all pediatricians, who, in co-operation with physicians and dentists, are applying a technique to evaluate medical service in one large segment of the profession. It is hoped that this and the recent study of the Commission on Hospital Care will be supplemented by other similar investigations in order that all facts on which physicians can intelligently plan a better and more equitably distributed form of medical care will be available.

Physical examination revealed little except tenderness in the epigastrium, without spasm or a mass. The tongue was heavily fissured, with smooth red edges.

The temperature was 98.6°F, the pulse 100, and the respirations 24. The blood pressure was 130 systolic, 80 diastolic.

The hemoglobin was 12.5 gm per 100 cc. The urine had a specific gravity of 1.018 and gave a + test for albumin. The serum protein was 5.9 gm per 100 cc. A gastrointestinal series revealed a large ulcer crater on the lesser curvature of the stomach midway between the cardia and angulus, which measured 3.5 cm at the base and was surrounded by a wide collar of edema. The remaining portion of the stomach and the intestines were normal. Gastric analysis yielded 120 cc of fluid with 7 units of free hydrochloride after fasting, 48 cc with 23 units after alcohol and 130 cc with 57 units after histamine.

The patient was maintained on a medical regime for a month, during which she gained weight and was subjectively improved. Re-examination of the stomach by x-ray showed the lesion to be unchanged.

An operation was performed on the forty-third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WADE VOLWILER: Two years' duration of ulcer symptoms in no way rules out the presence of a slowly growing neoplasm, for in many authenticated cases the patients have had symptoms for several years. The initial regime of diet and medication in the case under discussion gave imperfect relief of ulcer pain, and nausea with vomiting was a prominent feature. These symptoms are somewhat suggestive of gastric cancer. It is probable that the weight loss was due to simple starvation from anorexia and vomiting, rather than to the presence of widespread neoplasm. The tongue abnormalities suggest a prolonged inadequate diet.

The large size of the ulcer crater is statistically somewhat in favor of cancer, but statistics are not of great aid in single cases. I am not furnished with the necessary information relative to the peristaltic activity in the ulcer area, and to the presence or absence of rigidity of the gastric wall. I should like to know if the contour of the ulcer crater was perfectly smooth. The presence of free hydrochloric acid does not rule out cancer. Although the patient gained weight and had less discomfort, the ulcer crater did not change in size during a full month's careful observation under hospital conditions. Even

very large benign ulcers should show some diminution in size during this interval on a proper therapeutic program. It is possible that expert gastroscopy early in the hospital stay would have prevented a month's operative delay if neoplasm were actually present.

The choice of an exact diagnosis in this case is not possible. The important fact is that the ulcer did not change during a month's ideal regime, and therefore surgical extirpation was properly decided on and accomplished. The information is about equally divided in favor of a malignant and a benign lesion. If malignant, this was probably a slowly growing carcinoma, similar ulceration in a lymphoma occurs in this area, but is infrequent. Since I must make a choice, I shall cast my vote in favor of a gastric carcinoma.

CLINICAL DIAGNOSIS

Carcinoma of stomach?

Gastric ulcer?

DR. VOLWILER'S DIAGNOSIS

Carcinoma of stomach

ANATOMICAL DIAGNOSIS

Benign gastric ulcer, with penetration into pancreas

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: The first impression of the roentgenologist who examined this patient and also of the clinician on the ward was that they were dealing with a benign ulcer. It was decided to give the patient a therapeutic test of three weeks of adequate medical and dietary treatment. When this failed to produce any sign of improvement in the lesion, their confidence was shaken and they began to fear that it must be carcinoma. For this reason operation was undertaken.

On exploration a large ulcer was found on the lesser curvature, which was densely adherent to the pancreas. It proved impossible to separate the stomach from the pancreas, and a portion of the pancreas was therefore resected along with about two thirds of the stomach. It was fortunately possible to do this without interfering with the splenic vessels. The resected specimen showed a sharply punched-out ulcer crater measuring 3 cm in diameter. The base of the ulcer was formed by pancreatic tissue. Numerous sections from the walls of the ulcer showed no evidence of cancer.

ient of his affliction The danger arising out of de Kruif's article is best brought out by Commissioner Anslinger's own words

I fear a wave of Demerol addiction if physicians who read this article believe what I consider the reckless and dangerous statements made by de Kruif that the drug is free from addiction properties This is information somewhat similar to that which appears in the circular distributed by the manufacturer of Demerol to push sales Had this article been prepared on a strictly scientific basis, it would have sounded a strong warning about the danger of addiction Our files contain numerous cases of addiction involving the use of Demerol I cannot too strongly warn the members of your association about the danger of addiction to Demerol

The *Reader's Digest* is not noted for retracting erroneous statements that appear in its articles It might do well to start now by publishing Mr Anslinger's letter prominently in a subsequent issue

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CHASE — Harrison A Chase, M.D., of Brockton, died July 23 He was in his sixty-ninth year

Dr Chase received his degree from Harvard Medical School in 1905 He was a member of the American College of Physicians and a fellow of the American Medical Association

DJERF — Frederick J Djerf, M.D., of Fitchburg, died July 15 He was in his forty-fifth year

Dr Djerf received his degree from Tufts College Medical School in 1929 He was a member of the New England Obstetrical and Gynecological Society and the American College of Surgeons

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1946

RÉSUMÉ

DISEASES	JUNE 1946	JUNE 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	0	2	2
Chancroid	1	1	*
Chicken pox	1401	1282	1170
Diphtheria	21	15	7
Dog bite	1345	1266	1299
Dysentery bacillary	3	1	2
German measles	570	139	199
Gonorrhea	326	378	378
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	2	1	*
Malaria	56	92	1
Measles	7879	1409	3918
Meningitis, meningococcal	4	17	16
Meningitis Pfeiffer-bacillus	0	2	1
Meningitis pneumococcal	2	5	4†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	1	2	0†
Meningitis, other forms	0	1	2†
Meningitis, undetermined	7	4	5†
Mumps	538	1677	966
Pneumonia lobar	65	140	215
Salmonella infections	37	18	8
Scarlet fever	425	948	791
Syphilis	373	335	417
Tuberculosis pulmonary	205	192	275
Tuberculosis other forms	12	13	23
Typhoid fever	3	2	7
Undulant fever	3	6	5
Whooping cough	517	560	560

*Made reportable December 1943

†Four year average.

COMMENT

Diseases reported at an incidence above the seven-year median included chicken pox, diphtheria, German measles and measles

Measles was reported at a record high for the month of June but had decreased from the peak of 11,501 cases reported in May

Diseases reported below the median included poliomyelitis, meningococcal meningitis, mumps, lobar pneumonia, scarlet fever and whooping cough

Lobar pneumonia was again at a record low for the fifth successive month

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from Boston, 6, Brookline, 2, Chelsea, 2, Gloucester, 2, Lancaster, 1, Lowell, 2, Somerville, 1, Taunton, 4, Worcester, 1, total, 21

Dysentery, bacillary, was reported from Lexington, 2, total, 2

Encephalitis, infectious, was reported from Worcester, 1, total, 1

Hookworm was reported from Wellesley, 1, total, 1

Malaria was reported from Belmont, 1, Boston, 15, Brockton, 1, Chicopee, 1, Clinton, 1, Dedham, 2, Douglas, 1, Easthampton, 1, Everett, 1, Fitchburg, 2, Foxboro, 1, Greenfield, 1, Haverhill, 1, Hingham, 1, Lawrence, 2, Lunenburg, 1, Lynn, 2, Malden, 1, Marlboro, 1, Medford, 2, Merrimac, 1, Montague, 1, New Bedford, 1, Newton, 1, Oxford, 1, Salem, 1, Saugus, 1, Salisbury, 1, Springfield, 3, Stoneham, 1, Taunton, 1, Warren, 1, Watertown, 1, Worcester, 2, total 56

Meningitis, meningococcal, was reported from Bröckton, 1, Malden, 1, Newton, 1, Watertown, 1, total, 4

Meningitis, Pfeiffer-bacillus, was reported from Springfield, 1, total, 1

Meningitis, pneumococcal, was reported from Fall River, 1, Mattapoisett, 1, total, 2

Meningitis, streptococcal was reported from Springfield, 1, total, 1

Meningitis, undetermined, was reported from Belmont, 1, Haverhill, 1, Marblehead, 1, Millbury, 1, Saugus, 1, Weymouth, 1, Worcester, 1, total, 7

Psittacosis was reported from Cambridge, 1, total, 1

Salmonella infections were reported from Boston, 1, Cambridge, 4, Chelsea, 3, Lexington, 1, Lynn, 5, Malden, 4, Newton, 3, South Hadley, 1, Springfield, 1, Swampscott, 2, Winthrop, 9, Worcester, 3, total, 37

Septic sore throat was reported from Amesbury, 1, Boston, 3, Mansfield, 1, total, 5

Tetanus was reported from Methuen, 1, Pittsfield, 1, Quincy, 1, total, 3

Trichinosis was reported from Boston, 2, total, 2

Typhoid fever was reported from Lowell, 1, Somerville, 1, Worcester, 1, total, 3

Undulant fever was reported from Boston, 1, Hanson, 1, Haverhill, 1, total, 3

CORRESPONDENCE

BOOKS FOR DEVASTATED LIBRARIES

To the Editor During the war, the libraries of half the world were destroyed by the impact of battle and in the fires of hate and fanaticism Where they were spared physical damage, they were impoverished by isolation There is an urgent need — now — for the printed materials which are basic to the reconstruction of devastated areas and which can help to remove the intellectual blackout of Europe and the Orient

The need is so urgent, scientists working in Europe are so handicapped, that surely those of us working near well equipped libraries will be willing to sacrifice the convenience of an "office copy" in order to provide library facilities for less fortunate colleagues

There is need for a pooling of resources, for co-ordinated action so that the devastated libraries of the world may be restocked so far as possible The American Book Center for War Devastated Libraries Incorporated, has come into being to meet this need It is a program that is born of the

of child care is being created throughout the United States. Finally, it has shown that the only way for federal agencies to understand the problems of medical practice is to work with physicians.

DEMEROL IS HABIT FORMING

IN A letter to the editor of the *Journal of the American Medical Association*,* H. J. Anslinger, Federal Commissioner of Narcotics, calls attention to the work of experts of the United States Public Health Service and others who brought forth convincing evidence of the habit-forming properties of Demerol. He also refers to the article by Paul de Kruijff in the June issue of the *Reader's Digest* entitled "God's Own Medicine — 1946," which appeared under the headline "The pain-fighting power of demerol is as miraculous as that of morphine — without the opiates' danger of addiction."

"This article," Mr. Anslinger points out, "adroitly makes no reference to the work of Dr. C. K. Himmelsbach of the United States Public Health Service and Drs. Hans H. Hecht, Paul H. Noth and F. F. Yonkman of Detroit, all of whom warned of the danger of addiction." "Demerol," he continues, "was placed under federal narcotic control by the Congress because of evidence given before that body of its dangerous properties. Some of the persons referred to in de Kruijff's articles could have attended the hearings before the Ways and Means Committee and have testified as to what they thought about the drug, but they elected to remain silent."

Time and again, the general public has been treated to great "scoops" in newspaper and magazine articles by enthusiastic writers of popular science and medicine. Most successful among such writers have been those who dramatize the great advances in medicine, and their writings have proved extremely remunerative. It seems likely that they are often encouraged by the sales-promotion divisions of manufacturers, particularly those of companies that hold patent rights to the remedies in question.

Usually such articles, when properly written and carefully edited, serve the useful purpose of educating the public concerning what they may expect

from the medical profession. At times they also serve to stimulate the laggard physician to keep up with medical progress. Careful editing by scrupulous, well informed and critical medical authorities is, however, quite essential to assure that the public learns only established facts and is not treated to half-truths or to unwarranted or premature deductions based on enthusiastic interpretations of preliminary observations or of limited and uncontrolled studies.

Unfortunately the urge to scoop or to be sensational has often resulted in the substitution of drama for truth, and popular appeal has often been placed ahead of the public good. Readers are presented with half-truths or with what they want to hear rather than with the unadulterated facts concerning what has actually become available. The favorable aspects of discoveries are emphasized, whereas their limitations and their possibilities for harm are all too frequently ignored or minimized.

When a new discovery in medicine concerns an item of vanity, such as a cure for baldness or for gray hair, the medical profession should be interested chiefly in ascertaining that the possibilities for harm have not been overlooked. That is particularly true, for example, of the many remedies for obesity and the so-called "rejuvenators," which have been heralded with enthusiasm by popular writers.

Great harm may also be done by giving false hopes to the poor sufferers of incurable disease or by encouraging those who require prolonged observation and care with hopes for a rapid cure when such is not actually the case. These misconceptions on the part of patients often serve to break their morale and also to destroy confidence in their physicians, which often plays such an important role in their general welfare.

In the case of Demerol, the danger is quite clearly brought out by Mr. Anslinger. Patients having pain will insist on relief by "God's own medicine," with the *Reader's Digest's* assurance that it is without danger of addiction. Those already addicted to narcotics are also in great danger of substituting one addiction for another. This may prove quite profitable to those who control the German patents on Demerol, but it may turn out to be quite disappointing to the honest physician who is trying to help rid his pa-

*Correspondence. Addiction to Demerol and *Reader's Digest*. J. A. M. A. 131:937, 1946.

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SCLEREDEMA: A SYSTEMIC DISEASE*

BERT L. VALLEE, M.D.†

BOSTON

IN 1900, Buschke¹ described the case of a forty-six-year-old carriage painter who suffered from persistent brawny induration of the skin of the face, chest and upper extremities. Following influenza, firm, nonpitting edema started in the neck and spread centrifugally. There was marked chemosis. The patient did not appear ill, had lost no weight, had no fever and had no complaints other than immobility of the skin. Buschke thought this picture to be distinct from those of previously reported syndromes and called the disease "scleredema adultorum."

Many papers have since appeared in Germany delineating and expanding the original concepts,²⁻²⁹ and a few reports were published in other European countries in the following thirty years,³⁰⁻³⁵ but it was not until 1932 that the first note appeared in this country, when Epstein³⁶ reported 2 cases and reviewed the 41 cases previously described. Since then many publications have appeared,³⁷⁻⁷⁵ and the disease is readily recognized. The 4 patients to be described herein were all observed at Mount Sinai Hospital within the last six years.

CASE REPORTS

CASE 1 (M S H 454642 and 472542). A 35-year-old German was admitted on April 3, 1940, 11 weeks following a sore throat and tonsillitis with elevation of temperature that lasted a few days. Four weeks after the onset of sore throat, the patient noted thickening and tightening of the skin of the back of the neck, which gradually spread to involve the trunk, arms and upper abdomen. Intravenous typhoid vaccine and short-wave and calcium therapy were without benefit.

Physical examination revealed a well-developed man with masklike, oily facies. Both eyelids were puffy. There was slight restriction in opening of the jaws and protrusion of the tongue. The blood pressure was 120/80. The skin felt strikingly inelastic, thick, indurated and bound down to the underlying tissue over the face, chest, neck, back, abdomen and upper extremities. The hands were minimally involved, and the lower extremities were normal.

The urine was normal and had a specific gravity of 1.031. A blood Wassermann test was negative. The blood urea nitrogen was 10 mg per 100 cc, the sugar 80 mg, the cholesterol 280 mg, the cholesterol esters 165 mg, the phosphorus 3.8 mg, the calcium 11.2 mg, the total protein

6.5 per cent, and the creatinin 2.8 mg. A creatinin tolerance test showed no significant change. The basal metabolic rate ranged from -11 to -39 per cent. X-ray examinations of the chest, neck and skull were negative. Electrocardiographic tracings showed low voltage and an inverted T₄. Biopsy of the skin over the deltoid region revealed no abnormality. The sugar-tolerance curves ranged from 75 to 95 mg per 100 cc.

Desiccated thyroid was given in doses up to 0.7 gm daily, but without benefit. Hyperthermia was tried, and the patient experienced loosening of the skin following each treatment for several hours, but there was no lasting relief.

The patient was discharged after 3 weeks and was observed in the Out Patient Department for 1 year. On April 29, 1941, he was readmitted to the hospital for further study. During this interval there were only minor fluctuations in the stiffness and induration of the skin.

The findings on readmission were essentially those of the first admission. The hemoglobin was 88 per cent (Sahli) and the white-cell count 9950, with a normal differential count. The basal metabolic rate on two occasions was -4 and -10 per cent. A test showed sweating to be markedly reduced over the entire body. The sugar-tolerance curve was normal. The chloride was 595 mg per 100 cc, the alkaline phosphatase 10 K-A units, the albumin 5.1 gm, the globulin 1.6 gm, and the icteric index 6. The other blood chemical findings were essentially those during the first admission. Throat cultures revealed beta-hemolytic and alpha-hemolytic streptococci. The urine was negative, as were electrocardiographic tracings. A biopsy of the left deltoid region showed swelling of the collagen bundles of the corium and subcutaneous tissue. With *Kresleychiviolet* a faint pink-staining intercollagenous substance, such as that described by Freund³² was demonstrated. The histologic findings were interpreted as consistent with scleredema adultorum.

On the 13th hospital day, treatment with 3 cc of dihydro-tachysterol daily was begun, and after 2 days this dosage was increased to 5 cc. After 12 days of this therapy, the patient manifested severe toxic symptoms characterized by malaise and vomiting. The calcium blood level was 14.5 mg per 100 cc. The skin seemed to have softened, although there had been no dramatic improvement. The patient was discharged at his own request after 2 months of hospitalization.

Follow-up examination in December, 1944, showed the skin of the upper extremities to be hard and inelastic. The masklike facial expression was still present, although the cutaneous changes of the thorax, abdomen and neck had disappeared.

CASE 2 (M S H, O.P.D. 40-4027). The patient, a 16-year-old Puerto Rican girl, had been in good health until April, 1940, when she developed pneumonia with subsequent empyema necessitating surgical drainage. One month after recovery she developed sudden swelling of the back of the neck, face and scalp, with difficulty in moving the head from side to side. In a few days the swelling spread to involve the shoulders and upper arms.

Physical examination revealed a young girl with a hard edema in the areas previously described. The skin was taut, had a rubbery consistence and did not pit on pressure. There was no affection of the underlying muscles. The blood pres-

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combined interests of library and educational organizations, of government agencies and of many other official and non-official bodies in the United States.

The American Book Center is collecting and is shipping abroad scholarly books and periodicals which will be useful in research and necessary in the physical, economic, social and industrial rehabilitation and reconstruction of Europe and the Far East. The Center cannot purchase books and periodicals, it must depend on gifts from individuals, institutions and organizations.

Medical and scientific books and periodicals constitute the most important type of material needed and it is needed now. We feel sure that members of the Massachusetts Medical Society and other readers of the *Journal* will want to help their suffering colleagues in war-torn Europe and Asia.

WHAT IS NEEDED Scholarly books published in the last decade in general science and technology, medicine and the allied sciences, dentistry, chemistry, physics, biography, the social sciences, the fine arts and fiction of distinction. Scholarly scientific books will be especially welcome even if not the last edition of a standard work so long as the book has been published in the last decade. Periodicals in any of the above subjects, including runs of volumes, single volumes and even single issues. Large quantities of the more usual journals are needed, such as *Science*, *Proceedings of the Society of Experimental Biology and Medicine*, *Journal of the American Medical Association*, *Surgery, Gynecology and Obstetrics*, *American Journal of Surgery*, *New England Journal of Medicine*, *New York State Medical Journal*, *Southern Medical Journal*, *Journal of the Association of American Medical Colleges*, *American Journal of Public Health*, *U S Public Health Reports Weekly* and journals in the special sciences and clinical specialties. If in doubt, a list of titles available should be sent direct to headquarters before shipping, giving a rough idea of dates and volumes, the inquirer will be informed whether the material offered meets requirements.

WHAT NOT TO SEND State journals or journals of purely local interest other than those listed above, old transactions of medical societies, material of ephemeral interest, outdated textbooks and monographs, students' compends, annual reports or local state documents, material of doubtful importance published by commercial firms, schoolbooks, books for children or young people, light fiction, material of local interest and popular magazines.

How to SHIP All shipments should be sent *prepaid* via the cheapest means of transportation to the American Book Center, c/o The Library of Congress, Washington 25, D C. Although the Center hopes that donors will assume the costs of transportation of their materials to Washington, when this is not possible reimbursement will be made on notification by card or letter of the amount due. The Center cannot accept material that is sent transportation collect. Reimbursement cannot be made for packing or other charges beyond actual transportation costs. When possible, periodicals should be tied together by volumes. It will be helpful if missing issues are noted on incomplete volumes. It is hoped that many will feel that they can make part of their contribution the payment of transportation of material as far as Washington.

(Mrs.) EILEEN R. CUNNINGHAM, *Chairman*
Division of Medical Literature, American Book Center
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HUNGER EDEMA

To the Editor In the editorial "Avitaminosis and Hypoproteinemia in Starvation" appearing in the July 4 issue of the *Journal*, reference is made to the reports in the literature of the high incidence of so-called "hunger edema."

I was with an evacuation hospital that took over the Mathausen Concentration Camp in Austria shortly after its liberation in May, 1945. Our experience was slightly different from that reported elsewhere. Edema, regardless of a severe state of nutrition, was rare. We gave these persons plasma, whole blood and fluids. Within a few hours or days edema became intense. Many of the patients who had previously been merely a mass of dehydrated skin and bones developed a marked pitting edema extending over the entire

body. Their features were often unrecognizable. Restriction of fluids was necessary to relieve the edema. The blood protein levels before the onset of edema were usually low or normal. Under the Germans, the daily fluid intake had been so restricted that edema formation was impossible. Evidence of gross vitamin deficiency was rare, the only picture resembling that of beriberi.

ROY J. FOXKIN, M.D.

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NOTICES

ANNOUNCEMENTS

Dr John M. Barry announces that he will resume the practice of medicine in association with Dr. Z. William Colcoa at 215 Bay State Building, Lawrence.

Dr Philip S. Foisie announces the reopening of his office for the practice of surgery at 520 Commonwealth Avenue, Boston.

SEMINAR IN LEGAL MEDICINE

A seminar in legal medicine, sponsored jointly by the Department of Legal Medicine, Harvard Medical School, and the Massachusetts Medico-Legal Society, with the co-operation of the medical schools of Boston University and Tufts College, will be held during the entire week of October 7 to 12. The seminar will cover subjects of particular interest to medical examiners, coroners, pathologists and others interested in medicolegal investigations, and the attendance is limited to twenty. For further information write to Dr. William H. Watters, Harvard Medical School, 25 Shattuck Street, Boston 15.

AMERICAN COLLEGE OF PHYSICIANS

The twenty-eighth annual session of the American College of Physicians will be held from April 28 to May 2, 1947, at Chicago, Illinois. Dr. David P. Barr, of New York City, is president of the College and will be in charge of the program of general sessions and lectures. Dr. LeRoy H. Sloan, of Chicago, has been appointed general chairman and will be in charge of the program of hospital clinics and panels, as well as local arrangements, entertainment and so forth. Mr. Edward R. Loveland, executive secretary of the College, 4200 Pine Street, Philadelphia 4, will have charge of the general management of the session and the technical exhibits.

INDUSTRIAL HEALTH CONGRESS

As previously noted, the Seventh Annual Congress on Industrial Health, sponsored by the Council on Industrial Health of the American Medical Association, will be held in Boston during the week beginning September 30. Headquarters will be at the Copley Plaza Hotel, with some of the meetings scheduled for halls at Harvard University.

Preliminary plans call for meetings of committees and of the Industrial Health Council on September 28 and 29. The first day of the Congress will be given over to a symposium on lead poisoning and to an afternoon surgical conference. A state-society dinner and conference will climax the day. On Tuesday, October 1, there will be a morning symposium on problems in industrial medicine as viewed by labor, management and medicine. Elective conferences are planned for the afternoon, these will cover industrial physiology, administrative methods, aviation medicine and workmen's compensation. A Pan-American dinner and conference will be held in the evening. The third day will highlight medicine and industry in a physicochemical age, and also the place of physical fitness programs in industry, with the Bureau of Health Education of the American Medical Association contributing interesting data. A public dinner for health and welfare leaders, at which a nationally-known industrial leader will be the speaker, will climax the program.

The Congress this year is being co-sponsored by the Council of the New England State Medical Societies.

(Notices continued on page xv)

gs The skin of the feet was spared There was no pigmentation of the skin or scarring anywhere

On physical examination the eyelids were markedly puffed and distorted the face, which was mildly edematous The conjunctivas were swollen and edematous The upper respiratory passages, heart, lungs and abdomen were normal, and neurologic examination was not remarkable There was hard, nonpitting edema of the legs and thighs No pigmentation or scarring was present The feet were spared There was no acral edema The hemoglobin was 70 per cent (Sahl), the red-cell count 3,900,000, and the white-cell count 5000, with a normal differential count The urine was repeatedly negative, as was the blood Wassermann reaction The blood urea nitrogen was 8 mg per 100 cc, the sugar 75 mg, the chloride 595 mg, the cholesterol 292 mg, the cholesterol esters 205 mg, the carbon dioxide combining power 51 vol per cent, the phosphorus 3.4 mg per 100 cc, the calcium 9.5 mg, and the total protein 6.7 gm, with an albumin of 3.8 gm and a globulin of 2.9 gm The hippuric acid excretion was 6 gm, and the galactose excretion 1.5 gm An electrocardiogram revealed no abnormality An electroencephalogram was negative X-ray examination of the skull

disappears and the patient enters an asymptomatic period varying from several days to as long as three months The onset of the edema may be the initial manifestation of scleredema, or there may be a short prodromal period of malaise, myalgia and even low-grade temperature

The appearance of a patient with scleredema is so striking as to suggest the diagnosis immediately The face, neck, thorax, legs and buttocks present an extensive pale swelling The normal mobility of the face is lost The lines are obliterated by a dull, waxy swelling The lack of facial expression suggests the masklike facies of parkinsonism The conjunctivas are thickened and elevated, but the edema ends abruptly at the cornea The eyelids are especially involved (Fig 1), frequently being



FIGURE 1 Case 4

These photographs were taken in June, 1945 Note the marked eyelid changes and chemosis

was negative X-ray examination of the chest revealed no abnormality of the lungs or pleural cavities Fluoroscopy showed the horder of the right heart to be prominent with diminished pulsations, a fact that was confirmed by kymography Intravenous pyelography revealed slight ptosis of the kidneys There was no demonstrable abnormality in the urinary tract The basal metabolic rate was +11 per cent The sedimentation rate of erythrocytes was 29 mm per hour A skin test for trichinosis infection was negative A biopsy specimen taken from the leg showed nothing significant A urine concentration test gave a specific gravity of 1.030, and phenolsulfonphthalein excretion was normal

The patient had been admitted for diagnostic purposes She was afebrile on entry and there was no significant change in her condition during her stay No treatment was administered The disease process was considered to be scleredema adultorum, and the ultimate prognosis was thought to be good She was discharged after 3 weeks of hospitalization

CLINICAL MANIFESTATIONS

In most of these cases of scleredema a febrile illness preceded the onset of the disorder The infections have most frequently been influenza, sore throat, tonsillitis and scarlet fever It is interesting to note that in most cases the initial illness has been streptococcal in origin This acute infection

swollen and red The pallor of the edema is so pronounced that patients are often thought to be anemic, although the dead-white color of scleroderma is lacking The edema is hard and non-pitting On palpation the skin and subcutaneous tissue feel thickened and indurated The affected skin cannot be picked up in folds or creased Occasionally an erythematous or scaly rash affecting the arms and face is transiently present Closer examination of the affected areas reveals that the normal pits and skin markings are well preserved or exaggerated The dermal appendages are not affected

Scleredema most frequently begins in the nape of the neck and spreads to the face, thorax and shoulders Not infrequently the abdomen, lower and upper extremities and buttocks are involved More rarely the tongue and pharyngeal tissues are affected^{29 36 42} The tongue is described as immobile and large, the patient suffering from dysarthria Complaints of dysphagia are referred to scleredema of the pharynx Several observers have noted that

sure was 120/80. The remainder of the physical examination was not remarkable.

The urine was normal. The hemoglobin was 85 per cent (Sahli) and the white-cell count 6300, with a normal differential count. A blood Wassermann test was negative. The blood urea nitrogen was 13 mg per 100 cc, the sugar 75 mg, the calcium 10.6 mg, the phosphorus 4.0 mg, and the alkaline phosphatase 9 K-A units. The sedimentation rate of erythrocytes was not increased. The basal metabolic rate was +8 per cent. An electrocardiogram showed low voltage of the QRS complexes.

The patient was followed for 3 years in the Out Patient Department. She was given numerous hyperthermia treatments and felt considerably improved after each treatment. The swelling gradually receded but was still marked when the patient was last seen 3 years after the onset of the illness.

CASE 3 (M S H 519043 and 525942) A 37-year-old woman was admitted on April 14, 1944, about 8 weeks after the onset of edema of the face and neck. One month before the onset of these complaints all the teeth had been extracted. The extractions were followed by severe infection of the sockets, lasting for 1 week. Three weeks later edema of the neck, face and breasts developed, spreading to the back, chest and lower extremities. The upper extremities were never involved. The edema was unsightly but not discomforting. The patient was otherwise in good health.

Physical examination revealed edema of the face, conjunctivas, trunk, abdomen and lower extremities. The edema was remarkable in that it was firm and pale and did not pit on pressure. It was not dependent in location and had no relation to gravity, and there was no change in the course of the day. The edema was most marked about the face, especially the forehead, and was present to a moderate degree over the areas previously enumerated. There were marked chemosis and considerable lacrimation. The heart and lungs were not remarkable. The blood pressure was 110/90. A soft liver edge was felt approximately 1 cm below the costal margin. Neurologic examination was not remarkable.

Repeated urine examinations showed no protein or formed elements. The hemoglobin was 85 per cent (Sahli) and the white-cell count 4900, with a normal differential count. The erythrocyte sedimentation rate was 72 minutes. The venous pressure was 7 cm, and the circulation time (decholin) was 17 seconds. The basal metabolic rate was -6, -9 and -3 per cent. Repeated stool examinations revealed no parasites or occult blood. Phenolsulfonphthalein tests on two occasions showed 35 and 25 per cent excretion in 1 hour. The concentration test showed a maximal specific gravity of 1.030. A galactose-tolerance test showed an excretion of 0.85 gm. An oral hippuric acid test revealed an excretion of 3.8 gm. The initial total protein was 6.0 gm per 100 cc, and subsequent determinations were within normal limits. The albumin was 3.7 gm, the globulin 2.3 gm, the phosphorus 4 mg, the calcium 10 mg, the chloride 640 mg, and the cholesterol 300 mg per 100 cc. A bromsulfalein test showed no significant retention.

X-ray examination of the chest revealed an effusion occupying the lower portion of each pleural cavity. The size of the heart could not be determined. A flat plate of the abdomen showed general density, suggesting fluid. A number of electrocardiographic tracings revealed a regular sinus rhythm, with QRS complexes and T waves of extremely low voltage. A skin test for trichinosis was negative.

During the first 3 weeks in the hospital, the urinary output was high, but there was a gain in weight from 165 to 173 pounds. The patient was given injections of Mercupurin, which were effective in producing loss of weight. Nevertheless she remained quite edematous and 15 pounds above her usual weight. Desiccated thyroid was given in large doses, without result, although the basal metabolic rate rose to +9 per cent. Large amounts of human plasma were finally administered without significant effect. The patient was discharged essentially unimproved after 3 months of hospitalization, to return 3 months later for further study. During the interim the edema remained constant. She was readmitted on October 5, 1944.

Physical examination on readmission showed marked edema of the eyelids and conjunctivas. The skin over the previously mentioned areas was edematous and hard, although mostly over the breasts and back. It could not be lifted from the underlying structures, although there was no atrophy or pigmentation. There were many striae but no scarring over

the back and abdomen. The lungs and heart were not remarkable. The blood pressure was 110/70. The hemoglobin was 72 per cent (Sahli) and the white-cell count 5700, with a normal differential count. Urine examinations were always normal. The blood urea nitrogen was 17 mg per 100 cc, the total protein 6 gm, with an albumin of 5.9 gm and a globulin of 1.9 gm, the phosphorus 3 mg, the calcium 10.9 mg, the cholesterol 240 mg, the sodium 143.2 milliequiv per liter, the chloride 104.2 milliequiv, and the uric acid 3.6 mg per 100 cc. A blood Wassermann test was negative. The antifibrinolytic titer was zero. The Aschheim-Zondek test was negative. The visual fields were within normal limits. The basal metabolic rate was -2 per cent. Repeated Sulzowitch tests on the urine gave reactions within normal limits. Skin sensitivity to ultraviolet light was normal. Hippuric acid, phenolsulfonphthalein and cephalin-flocculation tests were negative. A creatinine-tolerance test was negative. Calcium excretion of a 3-day urine specimen of 2635 cc following a Bauer-Aub diet showed 230 mg calcium excretion, which is normal. A salt tolerance test was negative. Two 17-ketosteroid determinations were 12.0 and 16.6 mg per 100 cc, respectively, which are normal. The blood-iodine level was 5 gamma, which is normal. The sedimentation rate of erythrocytes was repeatedly normal.

X-ray examination of the chest showed enlargement of the cardiac shadow to the right and left. There was an enlargement of the right border with markedly diminished pulsation by fluoroscopy and kymography, suggesting a localized pericardial effusion. Right and left pleural effusions that had previously been present had disappeared. Examination of the long bones showed no abnormality. Examination of the sella turcica was negative. Electrocardiographic tracings showed a regular sinus rhythm, left-axis deviation and QRS of low voltage, changes seen in pericardial effusion.

A biopsy of the skin of the right breast showed changes compatible with the diagnosis of scleroderma adultorum. Staining with Kresley's toluidine blue, however, did not reveal an intercollagenous substance.

The patient's course was uneventful except for purulent conjunctivitis, the etiology of which was not discovered. Shitlump examination of the cornea revealed no abnormality. The temperature was normal throughout. There was both subjective and objective improvement. She was treated with effervescent urea, from which she had a good diuresis, but after 2 weeks of its use she became refractory to it and her weight became stabilized at 134 pounds. Because of previously reported pituitary disturbances in scleroderma adultorum,^{12, 25, 33, 35} anterior-pituitary extract (Ambionone) was given every 2nd day in 1-cc doses. The weight subsequently fell from 134 to 128 pounds, while the fluid intake remained restricted throughout. The skin softened noticeably, and the patient was discharged at her own request. The injections were continued three times weekly for 3 months following discharge.

When the patient was last seen in July, 1945, all the skin lesions had disappeared, x-ray examination of the chest was negative, and save for some residual chemosis there was no evidence of the previous disorder.

CASE 4 (M S H 535256) The patient, a 33-year-old woman, was first admitted on June 4, 1945. She had been well until the summer of 1943, when she developed generalized, hard, hrawny edema of the neck, face, abdominal wall, vulva, thighs and legs but not of the upper extremities and chest. A biopsy specimen was taken from the buttocks and was reported as scleroderma. The urine was said to contain formed elements and erythrocytes on several occasions during the early stages of her illness, but subsequently all examinations were negative and renal function was normal throughout. Bilateral pleural effusions developed and required continuous tapping for more than 9 months. Oliguria was an outstanding symptom. There was no cardiovascular disease. The patient was seen by various consultants in different hospitals over the course of 2 years, but no definite diagnosis could be arrived at. The blood chemical values, particularly the total protein, albumin and globulin determinations, were within normal limits at all times. The patient was given all types of available diuretics, without any therapeutic success. Among other measures autotransfusion with pleural fluid and renal decapsulation were performed without benefit. The generalized edema slowly disappeared over the course of months, although the patient was left with residual hrawny edema of the face, conjunctivas, eyelids and

eredema syndrome. Such intrathoracic effusions believe to be intrinsic features of the disease. This indicates, as do the reported hydrarthroses, that scleredema is not limited to the skin and subcutaneous tissue and may in fact present a puzzling picture to the internist.

INCIDENCE

In 1937, Touraine, Golé and Soulignac⁷⁰ were able to collect 70 cases from the literature. We have found a total of 99 reported cases and add 4 of our own, bringing the total to 103. In 97 cases in which knowledge of the sex is available, the patients were men in 33 and women in 64, an incidence of almost two to one in favor of women. An identical ratio reported by Touraine et al.⁷⁰ The greatest age incidence is in childhood and early adult life, as shown in Table 1. The oldest patient reported was

TABLE 1 Age Incidence

AGE	No. of CASES
37	27
Under 10	22
1-20	18
21-30	12
31-40	10
41-50	6
51-60	3
61 and over	3

sixty-eight years old.³⁰ The disease has also been observed in the early neonatal period.¹¹

PATHOLOGY

The squamous-cell and keratin layers of the epidermis present no abnormalities. The basal-cell layer may be alternately flattened out or heaped up. The superficial layers of the cutis usually show no feature other than slight perivascular infiltration.¹² Epstein³⁶ noted a band of connective tissue underlying the epidermis. The infiltrating cells are usually fibroblasts, lymphocytes and plasma cells.

The characteristic pathologic features are found in the deeper layers of the cutis.¹² The perivascular infiltration is more pronounced here, although it is variable and may not be at all striking. The collagen bundles are thickened to several times their usual diameter and form a firm fibrous band. Separating the collagen bundles and in interstitial areas throughout the cutis and subcutis are clear areas. There are also areas of fenestration about the blood vessels and hair follicles. With haematoxylin-eosin stain these areas appear empty. Freund¹² used *Kresylechtviolett*, which stained the tissues blue-gray but the material in these clear spaces a brilliant red. He also demonstrated small patches of this amorphous material in islands throughout the entire cutis. Both Voss²⁸ and O'Leary,⁵⁷ however, were unable to stain the interstitial material with *Kresylechtviolett*. This dye in one of our cases also failed to stain the clear areas, and in another case it was

only partially satisfactory. This apparent discrepancy is explained by the fact that the microscopic picture is variable. It probably varies with the stage of the disease, as noted by Epstein,³⁶ and may vary in different areas, retaining, however, the three major characteristics of perivascular infiltration, swelling of the collagen bundles and the presence of areas of fenestration.

The only autopsied case is that of Stenbeck.⁶⁵ He describes proliferation of connective tissue throughout the entire body, leading eventually to death through strangulation of the bowel. This patient, however, presented many unusual features, and the case cannot be accepted as an established one of scleredema.

ETIOLOGY

Buschke¹ was vague about the etiology in his first case. He suggested that the initial infection injured the lymph channels, producing elephantiasis of the skin. That the initial infection produces the agent responsible for the disease is the opinion of many contributors. Credence is lent to this thesis by the fact that the initiating infection is most frequently streptococcal in nature (Table 2). In

TABLE 2 Preceding Infections

DISEASE	No. of CASES
Influenza	24
Sore throat	9
Scarlet fever	8
Tonsillitis	6
Nephritis	6
Rheumatic fever	3
Respiratory infection	3
Fever	3
Pneumonia	2
Encephalitis	2
Pyoderma	2
Measles	2
Abortion	2
Wound infection	1
Dental infection	2
Otitis media	1
Erysipelas	1
Mumps	1
Typhus fever	1
No preceding infection	5

addition, in a number of cases the area of scleredema began in the region of the skin injured by the infection.²² 27 30 32 Guv⁴⁵ noted in 1 case that skin sensitivity tests for streptococci were markedly positive.

There is some evidence pointing to the endocrine organs as possible causative factors. No persistent changes in the basal metabolic rate have been described, but in a few cases x-ray evidence of tumor of the pituitary was evident.¹² 25 53 65 In one of these cases, which showed enlargement of the pituitary bed and destruction of the posterior clinoid processes, Schreus²⁵ claims to have experimentally demonstrated a substance in the blood and urine having the same effect on water metabolism as does the extract of the posterior pituitary gland. Selye⁷⁶

the scleredema frequently begins in that area, which has been affected by the previous febrile illness. It is a characteristic feature of the disease that the hands and feet are spared.

The skin is not the only system affected. Cases 3 and 4 showed hydrothorax, and hydrarthrosis was found by Voss,²⁸ Schnitzer,⁶³ and O'Leary.⁵⁷ The patient's complaints usually relate either to the facial edema or to the immobility of the skin. Not infrequently the stiffening of the skin of the thorax restricts chest motion,²³ producing a sensation of dyspnea. Occasionally movements of the extremi-

Except in a few cases in which the initiating febrile illness was nephritis,^{13, 19, 45, 52, 63} the urine consistently shows no abnormality. The total urinary output has not often been recorded, but Buschke⁹ noted that during the edematous phase there was oliguria, with regression of the edema he observed marked diuresis.

The blood is usually within normal limits, showing neither anemia nor leukocytosis. The sedimentation rate is normal or at best slightly elevated.

The basal metabolic rate has been reported as being high⁶¹⁻⁶³ and as being low.⁴⁵ In most cases,

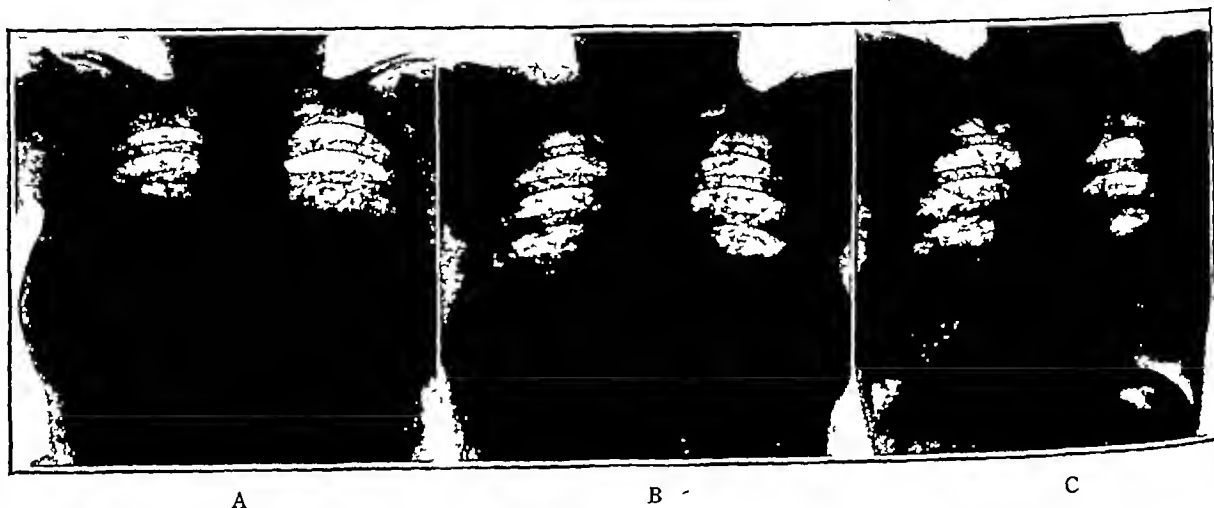


FIGURE 2 Roentgenograms in Case 3

A — This film was taken on admission in April, 1944. B — This film was taken during second admission and shows disappearance of the pleural effusion but persistence of the pericardial effusion, particularly prominent at the right pericardial border. C — This film was taken in June, 1945, when the resolution of the cutaneous manifestations was virtually complete. The patient never had clinical symptoms referable to intrathoracic effusions.

ties are hampered. The maximal area of skin involvement is reached early in the disease, and the course thereafter is one of slow regression. Regression usually begins in the areas last affected and persists longest in those first involved, particularly the neck, face and scalp. Complete resolution has occurred in few cases in less than a month.^{17, 29} In most cases regression takes longer than six months, and not infrequently islands of scleredema are left, slowly resolving after a period of years. It is frequently stated that the disease is self-limited, but the case reported by Adler² showed evidence of scleredema of the eyelids after twenty years. In the case described by Hoffmann,¹⁵ extensive edema persisted for fifteen years. The prognosis for life and function is excellent, and ultimate complete recovery can be expected, yet the duration of the edema is unpredictable.

In a number of cases relapses have occurred.^{2, 3, 36, 57} These characteristically occur after a long free period, — thirteen years in Epstein's³⁶ patients and twenty years in one of O'Leary's.⁵⁷

however, it is in the normal range, as in the present series.

In these cases the total protein, albumin, globulin, chloride, glucose-tolerance, blood-sugar, calcium and phosphorus levels were normal. The 17-ketosteroid excretion in Case 3 was normal, as was the blood-iodine level. No significant blood chemical aberrations have been noted by other authors.^{17, 43, 57, 60, 63}

Electrocardiograms showed QRS complexes of low voltage.

X-ray examination of the chest has only rarely been included in clinical reports but usually shows no abnormality. Nevertheless, the patient in Case 3 had a right pleural effusion when first seen and later developed a loculated effusion along the right border of the heart. Both these effusions regressed as the process cleared up. In Case 4, there were massive bilateral pleural effusions during the initial phase of the disease (Fig 2). To our knowledge, these are the first cases in which pleural and pericardial effusions have been reported as part of the

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thinks that topical application of estrogens in mice produces a pathologic picture resembling that of scleredema

Helfand,⁴⁶ struck by the clinical resemblance between trophedema and scleredema, suggested that the pathogenesis might be disease of the peripheral nerves. He demonstrated with Spielmeyer and Weigert-Pal stains disintegration of the myelin sheaths of the subcutaneous nerve fibers.

At present, however, there is insufficient material available to permit a reasonable opinion of the etiology.

DIFFERENTIAL DIAGNOSIS

There are few cases of scleredema that have not at one time been diagnosed as scleroderma, but the differentiation may be easily made on clinical grounds. The hands, so frequently diseased in scleroderma, are spared in scleredema. The skin similarly does not show the atrophy and contractions or areas of pigmentation and depigmentation seen in scleroderma. Whereas scleroderma frequently produces disease of the lungs, esophagus and heart and decalcification of the bones, these changes are never seen in scleredema. Finally, scleredema is a benign and self-limited disease and is usually seen in the stage of regression.

Myxedema may be differentiated by means of the basal metabolic rate, the blood cholesterol values, the general appearance and behavior of the patient and finally the lack of response to desiccated thyroid.

Dermatomyositis occasionally gives rise to a difficult diagnostic problem. Touraine et al.⁷⁰⁻⁷² claim that a number of cases described as acute dermatomyositis are actually scleredema. Nevertheless the presence of muscle pain, fever, a high sedimentation rate and the widespread erythematous skin lesions occasionally seen in dermatomyositis and the weakness and atrophy that are constant features of the disease are not seen in scleredema. Finally, dermatomyositis is usually a progressive and crippling disease. Recovery, which is not frequent, is attended by atrophy and incapacity.

Trichinosis may be ruled out on the basis of the elevation of temperature, the marked muscle tenderness, eosinophilia and the localization and nature of the edema. The skin and complement-fixation tests serve as laboratory aids in the differential diagnosis.

Edema from cardiac and renal as well as hepatic disease is readily differentiated by simple clinical grounds.

TREATMENT

The treatment of the disease is unsatisfactory. The disease appears to follow its own course, unaffected by any therapeutic agents. Our therapeutic trials included desiccated thyroid, dihydro-

tachysterol and anterior pituitary extract. These agents did not contribute markedly to the patient's recovery. O'Leary⁸⁷ claims beneficial results from fever therapy, but his results with it, as well as our own, are not striking. It is also doubtful whether eradication of a focus of infection can be expected to influence the course of the disease. Further studies of the pathogenesis of the process may elucidate the therapeutic problem.

DISCUSSION

The name "scleredema adultorum," as given by Buschke,¹ does not seem appropriate. The term implies that this is an illness seen only in adults, yet the statistics on age distribution (Table I) show that it is most frequently observed in children and adolescents, who account for 50 per cent of all cases on record. Calling the disease "scleredema" without reference to the age groups affected seems more in keeping with the statistical facts.

The recognition of the disease is important because of the excellent prognosis for function and life. The process always undergoes spontaneous regression, in contrast to scleroderma and dermatomyositis, with which it is frequently confused. The pleural effusions in 2 of our cases and the electrocardiographic changes are of interest, particularly since the intrathoracic effusions receded simultaneously with improvement of the cutaneous changes.

Cases of scleredema undoubtedly come under the observation of internists. A relatively small number of cases have been reported in the literature to date. Nevertheless, we have observed and followed 4 cases ourselves within a relatively short period. It seems to be a reasonable conclusion that the disease is not so infrequent as might be suspected.

Any case presenting obscure forms of edema should be suspected, and a detailed history may aid in ascertaining its true cause.

SUMMARY

Scleredema was first described by Buschke. Since his original description 99 cases have appeared in the literature, to which we add 4.

The disease is characterized by firm, nonpitting edema, affecting usually the face, neck, scalp, conjunctivas, thorax, occasionally the arms and more rarely the legs, sparing the hands and feet. Pleural effusions, pericardial effusions and hydrarthroses also occur. The pericardial effusions may be localized. The electrocardiogram shows low voltage of the QRS complexes.

Complete recovery can be expected over a period varying from several months to many years.

Young people are affected more frequently than those in the older age groups. Women are affected twice as often as men.

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Muscle tenderness was present in all the cases with bulbar involvement and in 6 of those without it, total of 16 cases. The muscle groups in which tenderness was found, in the order of frequency, were the hamstring muscles, the posterior calf muscles, the quadriceps muscles and the biceps muscles. It was interesting that tenderness of the muscles of the upper extremities was found in only 3 cases, although paralysis of the upper extremities occurred in 9 patients. One of the 2 patients without muscle tenderness was admitted three and a half weeks after the onset of his illness, and the other showed only involvement of the upper extremities, primarily the abductor muscles of the shoulders. It was also of interest that many more patients showed muscle tenderness than complained of muscle soreness. The tenderness persisted from a few days to weeks.

Fever was present in all cases but 1, which was that of the patient who entered the hospital late in the course of his disease. The height and length of the fever was variable. The temperatures generally ran from 100 to 103°F, but in 3 of the bulbar-involvement cases it was 104°F. Death occurred in 2 of these. So long as the temperature remains elevated, one cannot be certain how much more progression of the disease process there will be. In the bulbar-involvement cases this factor was of prognostic significance.

Muscle spasm was seen in no case with the patient at complete rest. There was no attempt to study muscle spasm by means of the electromyograph or by chronaxie measurements, so that any evidence of muscle spasm was that judged on a purely clinical basis. When certain muscles were placed on stretch, pain and spasm were generally elicited, their principal locations being the neck, back, hamstring muscles and posterior calf muscles. They were not, however, always elicited in paralyzed muscles. In the cases in which the tibialis anticus muscle and the abductor muscles of the shoulder were involved, passive stretching produced neither spasm nor pain. As pointed out by Moldaver,¹ muscle spasm in anterior poliomyelitis is a complex phenomenon, the result of a combination of factors — namely, a normal stretch reflex, meningeal irritation of the posterior roots, an increase of normal tonus in healthy and strong muscles or muscular fibers opposed to weak or paralyzed muscles, and lesions of the dorsal-root ganglions and posterior horns.

Reflex changes were not listed because of their variability and changeability. In most cases with complete muscle paralysis deep reflexes were absent in the involved area, but 1 of the cases with extensive paralysis showed hyperactive deep reflexes throughout. In another case with fairly extensive involvement there were no reflex changes. The reflexes in the same patient often varied from day to day. This was particularly true in the patients with muscle tenderness and weakness but no residual

paralysis. As the muscle tenderness disappeared and strength returned, the reflexes became normal. No pathologic reflexes were obtained. There was no evidence of cortical involvement in any patient.

Sensory changes were elicited in only 1 patient. A summary of this case is given below.

The spinal-fluid findings are listed in Table 3. Only the cell counts and total proteins are recorded. Sugar determinations and Wassermann reactions

TABLE 3 Spinal-Fluid Findings

No. of Case	CELL COUNT			TOTAL PROTEIN	DAY OF ILLNESS
	TOTAL CELLS	POLY-MORPHO-NUCLEAR CELLS	LYMPHO-CYTES		
				mg / 100 cc	
Cases with bulbar involvement					
1	495	470	25	65	4
2	9	2	7	48	5
3	10	0	10	48	5
4	10	0	0	74	7
5	14	0	10	74	9
6	14	0	14	31	5
7	5	0	14	31	8
8	22	1	5	67	4
9	1	0	21	43	7
10	0	0	1	20	4
11	0	0	0	15	8
12	9	2	7	33	21
13	25	1	24	48	5
14	400	72	328	47	10
15	5	1	4	54	4
16	13	4	9	105	15
17	3	2	3	50	3
18	1	0	3	150	10
	1	0	1	270	28
Cases without bulbar involvement					
11	21	0	21	43	5
12	110	15	95	14	7
13	85	10	75	43	5
14	2	0	2	44	25
15	2	0	2	48	3
16	17	1	16	43	9
17	41	2	39	36	3
18	37	0	37	36	5
	2	0	2	43	4
	3	0	3	37	10
	0	0	0	39	20
	1	0	1	39	32
	1	0	1	39	42
In cases 1 and 8 differential expressed in percentages					

are omitted, since the former were either within normal limits or slightly elevated and all the latter were negative. The day of withdrawal of the spinal fluid and its examination is recorded in terms of the onset of the disease.

Repeat spinal-fluid examinations were done in all cases in which the first examination revealed a normal cell count. In 7 cases with bulbar involvement, the spinal fluid obtained on admission showed a normal cell count or one below 10. In the group without bulbar involvement, the initial spinal fluid was normal in 3. One of these patients, however, was admitted late in the course of his illness, and since normal cell counts are not unusual at that time, it was believed that this case should be omitted in the calculation of the percentage. The remaining spinal fluids were obtained from patients in the first week of their illness. Thus, 53 per cent of the spinal fluids obtained on admission showed essentially normal counts — in 7 of the cases with bulbar involvement

SOME UNUSUAL FINDINGS IN AN EPIDEMIC OF ANTERIOR POLIOMYELITIS*

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DURING the months of March and April, 1945, a southern army post experienced a short but explosive outbreak of anterior poliomyelitis. Within a period of twenty-five days, 18 patients suffering from poliomyelitis were admitted to the hospital. There were 3 other cases that were considered to be preparalytic in type, but since the diagnosis was questionable, they are omitted from this discussion.

Anterior poliomyelitis is usually a disease of late summer and early fall. Winter epidemics have been described, but this outbreak cannot be so classified. The weather was unusually warm for the time of year, even though it is taken into consideration that the camp is situated in the southern part of the country, indeed, the temperatures approached those occurring in the summertime.

The diagnosis of acute poliomyelitis was confirmed by pathological studies, autopsies being performed in the 3 fatal cases. Histologic sections of the spinal cord and medulla revealed lesions characteristic of anterior poliomyelitis. Also, poliomyelitic virus was recovered from the central nervous system of 1 of the patients.*

All the cases occurred in soldiers, whose ages ranged from eighteen to thirty-three years, all but 3 were between eighteen and twenty-one years old. This camp has approximately 30,000 troops, most of whom are recruits, largely infantrymen. Some of those who contracted the disease lived outside the camp, although the great majority were stationed on the post. The post is located four miles from a city with a population of 40,000, and traffic between the camp and city is extensive. In spite of this, no cases occurred in any of the civilian population. It is not the purpose of this paper to discuss any epidemiologic aspect of this outbreak, but it should be stated that there was no personal contact between any of the patients.

The patients afflicted with the disease in this epidemic showed some unusual findings. There were 10 (55 per cent) with bulbar involvement. There were 3 deaths, all in cases with bulbar involvement and all caused by failure of the respiratory center. Also of considerable interest were some unusual spinal-fluid findings. This subject is discussed in detail below.

In Table 1 are detailed the symptoms and their frequency of occurrence. As can be seen, headache was the symptom most commonly noted, but in no case was it severe or marked, nor was it the chief complaint in any case. In a few cases direct questioning was necessary to elicit this symptom. Muscle pain, backache and dysphagia were the next most

frequent symptoms. The muscle pain was described in the majority of cases as "soreness" or "aches," and in some cases as an acute, severe pain. There were no shooting pains, such as those experienced in radiculitis. Dysphagia varied in intensity. Some patients were completely unable to swallow, others were able to swallow small amounts of liquids and

TABLE 1 Symptoms

SYMPTOMS	No. of Cases
Headache	12
Muscle pain	11
Backache	10
Dysphagia	10
Nausea and vomiting	6
Voice change	5
Muscle weakness	5
Fever	5
Chilliness	3
Sore throat	3
Abdominal pain	1

soft, mushy foods, generally washed down with liquids. Those who were able to swallow liquids tired easily, and it required an appreciable effort for them to swallow. The listing of stiffness of the neck as a symptom refers to subjective stiffness as reported by the patients, not to objective findings of stiffness, which were much more frequent (Table 2).

The physical findings have been divided into two groups, those in cases with bulbar involvement and those without it. Cranial nerves were affected in all

TABLE 2 Physical Findings

FINDING	No. of Cases
Cases with bulbar involvement	10
Fever	10
Uvula paralysis	10
Muscle tenderness	8
Stiff neck	5
Paralysis of muscles of the extremities	4
Facial paralysis	4
Weakness of muscles of the extremities	1
Weakness of sternomastoid muscle	1
Injected pharynx	1
Weakness of muscles of jaw	1
Cases without bulbar involvement	8
Weakness of muscles of the extremities	7
Fever	7
Paralysis of muscles of the extremities	6
Muscle tenderness	4
Stiff neck	1
Injected pharynx	1

bulbar cases, and paralysis of the extremities occurred in certain cases of both groups. The latter was generally mild. Of the cases with bulbar involvement, 5 showed no evidence of actual paralysis, but in 4 of these there was peripheral muscle weakness. The patient who showed no evidence of cord involvement died within a week after the onset of his illness.

*This work was done by the Commission on Neurotropic Virus Diseases, Office of the Surgeon General, United States Army.

ients with bulbar involvement who survived were able to swallow after a period of two weeks, but 5 of them had some residual. Two had slight dysphagia. Of these, one had a mild facial paralysis and the other a slight involvement of the sternomastoid muscle on one side. The 3 remaining patients had paralysis of the peripheral muscles. Of the 8 patients without bulbar involvement, 7 had some residual peripheral paralysis, although in each case improvement occurred. In 1 case there was complete recovery.

DISCUSSION

A short but violent outbreak of poliomyelitis occurring in adults has been presented. Poliomyelitis is primarily a disease of childhood. There has, however, been a gradual shift toward older age groups in poliomyelitis in both rural and urban populations in the last twenty years.⁵

This particular epidemic was characterized by a high incidence of bulbar-involvement cases. Stebbins et al.⁶ reported on an outbreak of 20 cases, 13 of which were of the bulbar type, 12 of these terminated fatally. The incidence of bulbar involvement varies with different epidemics. Lemmon,⁷ in an analysis of 49 cases occurring in an epidemic in Pennsylvania, reports an incidence of bulbar involvement of 12 per cent. Fischer et al.⁸ also report an incidence of 12 per cent, in a Toronto epidemic. Generally speaking, the incidence of bulbar involvement varies between 5 and 10 per cent.

The relation between tonsillectomy and bulbar poliomyelitis has been definitely established. None of the patients with bulbar involvement in this series had had a recent tonsillectomy and the proportion of those patients who had had tonsillectomy in the past was no greater than that of those without it.

Of considerable interest was the large proportion of patients with no increase in cells in the cerebrospinal fluid. On the initial examination 53 per cent of the spinal fluids showed normal cell counts. It had been noted that the usual findings in the cerebrospinal fluid in cases of anterior poliomyelitis are an increase in cell count and a slightly elevated protein during the first week, with a gradual decrease in cells to the third week and with a gradual increase in total protein.⁹ Cases without an increase in the cell count, however, have been reported,¹⁰⁻¹² and the incidence of cases without cellular response in the spinal fluid has been estimated at 12 per cent.¹¹ In the Los Angeles epidemic of 1934, approximately 33 per cent of the patients had normal cell counts.¹² Similarly, Jensen¹³ has reported 36 per cent of 3340 cases occurring in Denmark with normal cell counts.

Of particular interest is the case discussed above. The albuminocytologic disassociation is obvious. As is well known, this is a cardinal finding in the Guillain-Barré syndrome (infectious polyn neuritis). It will also be noted that in Cases 3, 5 and 9 this disassociation was also present. Cases of infectious

polyn neuritis occurring during poliomyelitis epidemics have been reported.¹⁴ An autopsy performed in Case 3, however, revealed the typical pathologic findings of poliomyelitis.

These observations demonstrate the difficulties encountered in the differential diagnosis of poliomyelitis and the Guillain-Barré syndrome. Different clinical criteria have been mentioned in numerous publications, they concern the mode of onset, the distribution of the paralyses and the laboratory findings. Progressive paralysis with diffuse symmetrical involvement, involvement of the facial nerve and albuminocytologic disassociation have been brought forth as differentiating the Guillain-Barré syndrome from poliomyelitis. The usually favorable outcome has also been pointed out as a differentiating point. Recent statistics, however, show the occurrence of a high mortality rate in polyn neuritis.¹⁵ On the other hand, complete recovery following an attack of poliomyelitis is frequently observed. It will be noted in the case reported above that many of the features of the Guillain-Barré syndrome were present. The course of the disease, however, was not that usually seen in this syndrome. Jervis et al.¹⁶ reported a case in which the clinical manifestations and laboratory findings that are considered typical of the Guillain-Barré syndrome were seen and in which autopsy indicated acute poliomyelitis. They believe that differentiation based on clinical symptoms, observations of the spinal fluid and the final outcome is open to question and that this raises the problem whether the two diseases are distinct entities or different clinical manifestations of the same agent. The point can only be settled from an etiologic point of view by isolating the poliomyelitis virus or another virus from patients with infectious polyn neuritis.

SUMMARY

The symptoms and physical and spinal-fluid findings in a short but explosive epidemic of anterior poliomyelitis are described.

An unusually high percentage of cases with bulbar involvement occurred.

A large percentage of the cases failed to show the cellular response usually seen in the spinal fluid in poliomyelitis.

The albuminocytologic disassociation described in the Guillain-Barré syndrome was found in 3 of the 18 cases in this series.

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and in 2 of those without it. Of this group of 9 cases there was an elevated total protein in 6, although 2 (Cases 2 and 15) showed only a slight elevation. Repeat spinal-fluid examination in this group done within a few days after the original examination showed an increase in cells in 5 cases. All but 2 showed some abnormality in the cerebrospinal fluid after repeated examinations.

The pathologic process and distribution of the virus in the central nervous system in cases of poliomyelitis are more widespread than the amount of paralysis indicates. All parts of the central nervous system appear to be involved to some extent, but the changes indicative of injury or destruction of nerve cells are generally found in the motor nerve cells of the brain stem and spinal cord. The large, deeply staining anterior-horn cells of the cord seem to be most vulnerable ones.

In the case reported below, there was extensive sensory involvement, as well as motor involvement, and an almost complete transverse myelitis.

CASE 10 A 28-year-old soldier was well until 2 days before admission to the hospital, when he developed general malaise, felt feverish and had generalized muscular aches. The following day he developed dysphagia and noticed a change in the quality of his voice. Attempts to swallow even fluids were followed by regurgitation through the nose. Later on that day he noticed some weakness of the left arm.

Physical examination revealed stiffness of the neck and back, a positive Kernig's sign and weakness of abductor muscles of the left shoulder. There were no reflex or sensory changes. The temperature was 102°F, the pulse 100, and the respirations 22.

For the next 2 days the patient continued to run an elevated temperature with little change in the general picture. He was unable to swallow even liquids and was given 1000 cc of pooled plasma, together with 5 per cent glucose and normal saline solution, up to 3500 cc daily. On the 3rd hospital day he developed complete paralysis of both lower extremities. He was found to have paralysis of the bladder and of the rectal sphincter. There was loss of the abdominal and cremasteric reflexes. The deep reflexes of the lower extremities were absent. There was no plantar reflex on either side. Position sense in the lower extremities was completely lost. There was also diminished tactile sensation corresponding to the level of the 2nd lumbar segment. Pain and temperature sensations were unaffected. There was weakness of the abdominal muscles and the abductor muscles of the left shoulder. Closed drainage of the bladder was instituted.

The patient continued to run an elevated temperature for 6 more days. His condition remained much the same during that period, after which he began to show gradual improvement. On the 12th hospital day he was able to swallow liquids, then soft solid foods. On discharge to an Army medical center for poliomyelitis 6 weeks after admission, he still had paralysis of the bladder, but the tone of the rectal sphincter had improved. There was return in function of the abdominal muscles and many muscle groups of the lower extremities, although there was still fairly extensive involvement. The abductor muscles of the left shoulder were much the same as on admission.

A report from the medical center showed paralysis of the lower extremities involving a diffuse group of muscles. There had been moderate improvement, but there was still considerable involvement of the right gastrocnemius muscle. Bladder paralysis was still present, but function had recovered sufficiently so that the use of a catheter was no longer necessary. The rectal sphincter had returned almost to its normal tone. This report covered the status of the patient 7 months after the onset of his illness.

Approximately 50 per cent of the patients in this series received both pooled plasma and penicillin.

Plasma was given in doses of 500 to 1500 cc. Penicillin was given intramuscularly, with an average total dosage of 1,680,000 units.

The evaluation of any therapeutic measure in anterior poliomyelitis is extremely difficult. In any such appraisal it must be borne in mind that a relation between the severity of the earlier symptoms and the ultimate appearance of the paralysis is inconstant; the death rate and the amount of residual paralysis vary greatly from place to place and in different epidemics. Furthermore, none of our patients were admitted in the preparalytic stage. So far as could be determined, neither plasma nor penicillin had any effect on the course of the disease. Convalescent poliomyelitis serum has been used in preparalytic states of poliomyelitis without benefit,¹ so that it is not surprising that no therapeutic results were obtained with pooled plasma given when paralysis or paresis had already set in. In addition, penicillin is reported to have no effect on the poliomyelitis virus.^{2, 4}

The hot-pack treatment, as advocated by Sister Kenny, was carried out on all but 2 patients. The patients with involvement of the lower extremities were placed on a mattress stiffened by a board placed over the springs and so placed that there was a distance of several centimeters between it and the foot of the bed. The soles of the feet rested against the footboard, and the heels were in the space between it and the mattress. When muscle tenderness and pain cleared, physiotherapy, including baking, massage and passive and active motion, were instituted. There was little doubt that hot packs definitely diminished the muscle soreness and pain. No plaster casts or splints were used. The cases with involvement of the upper extremities showed only moderate or slight paralysis, and pillows were used for support.

For the patients unable to swallow, tube feeding was used, but in the first few days of the illness, when the temperature was elevated and the patient was acutely ill, this was not done, but instead fluids were given parenterally. It was believed that tube feeding during the acute phase caused a marked increase in pharyngeal secretions, requiring constant suction. In no case was tube feeding necessary for longer than two weeks. In 2 of the 3 fatal cases the Drinker respirator was used when the respiratory center became involved. It had no effect on the ultimate outcome, although life was prolonged for about twenty-four hours.

The patients could be followed only for seven weeks. Those who had residual paralysis were transferred to an Army and Navy general hospital for further treatment.

There were 3 deaths, all occurring in bulbar involvement cases, and all from failure of the respiratory center. Thus, there was a 16 per cent mortality in the series as a whole and a 30 per cent mortality in the cases with bulbar involvement. The 7 pa-

ients with bulbar involvement who survived were able to swallow after a period of two weeks but 5 of them had some residual. Two had slight dysphagia. Of these one had a mild facial paralysis and the other a slight involvement of the sternomastoid muscle on one side. The 3 remaining patients had paralysis of the peripheral muscles. Of the 8 patients without bulbar involvement, 7 had some residual peripheral paralysis, although in each case improvement occurred. In 1 case there was complete recovery.

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TETANUS, WITH DEATH DUE TO ASEPTIC DURAL SINUS THROMBOSIS

Report of a Case

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THE following case of tetanus is reported because of several unusual features, one of which—aseptic dural sinus thrombosis—was apparently the cause of the fatal outcome.

CASE REPORT

P. G., a 6-year-old boy, entered the Elliot Hospital on September 1, 1945, with the chief complaint of difficulty in swallowing of 1 week's duration. Three weeks prior to entry, a wood splinter penetrated deep into the left anterior tibial area. Part of the splinter was removed and the wound was dressed at home. The patient was well until 1 week prior to admission, when a "frozen" expression appeared on his face and he had slight difficulty in swallowing. Four days prior to entry, there were painful muscular contractions at night. On the day of admission difficulty in walking developed.

The family and past histories were noncontributory. The patient had had measles as an infant. He had had no inoculations or immunizations.

Physical examination disclosed a well developed, well nourished and fairly well hydrated boy, who was alert and co-operative but somewhat apprehensive. Skin turgor was good. The skin was tightly drawn over the contracted facial and abdominal muscles. All the muscles were hypertonic and resisted passive motion. The neck was slightly retracted and the back was slightly hyperextended. All deep tendon reflexes were hyperactive. Kernig and Brudzinski reflexes were markedly positive. There was severe pain on attempted flexion of the neck, which was extremely stiff. The Babinski reflex was negative. Trismus and risus sardonicus were present. The mouth could be opened to 1 cm. between the teeth anteriorly. There was a nearly healed, nontender stab wound 3 mm. in diameter on the left anterior tibial area.

The red-cell count was 4,960,000 and the white-cell count 13,800, with 81 per cent adult and 1 per cent young neutrophils, 16 per cent lymphocytes, 1 per cent monocytes and 1 per cent eosinophils. The hemoglobin was 13.9 gm. Blood Hinton and Mazzini tests were negative. The patient was incontinent, and no urinalysis was done on admission. A lumbar puncture was done shortly after entry. The spinal-fluid sugar was 88 mg. per 100 cc., and the protein 18.7 mg. Pandey's reaction was negative, and the gold-sol curve was normal. Culture of the spinal fluid showed no growth.

The wound was excised and sodium perborate dressings were applied. Histologic examination of the excised area showed granulation tissue beneath an intact epidermis. Yellow foreign material, probably of vegetable origin and surrounded by large foreign-body giant cells and chronic inflammatory exudate cells, was seen. Gram stain showed large numbers of gram-positive bacilli, thought to be tetanus bacilli, and gram-positive cocci near the foreign bodies and in the adjacent soft tissue.

A diagnosis of tetanus was made, and treatment was begun shortly after entry. An initial dose of 40,000 units of tetanus

antitoxin was given intramuscularly into the buttocks. Forty five milligrams of Nembutal was given at entry and 33 mg. every 3 hours thereafter. Sodium luminal in doses of 65 mg. was given intramuscularly for acute spasm when needed. The patient was placed in a dark, quiet room. Hydration and dietary status were maintained by a special liquid for mola taken through a straw. The formula was based on whole milk with added Dextrinmaltose, sodium chloride, vitamin B complex and vitamins A, D and C. Other nourishing liquids and water were given by mouth as the patient tolerated them.

On the 2nd day, more frequent and severer painful muscular spasms of a generalized nature began, and the temperature rose to 101.8°F. Swallowing seemed easier. The abdominal and limb muscles were more spastic, and the neck and back more rigid. A dose of 10,000 units of tetanus antitoxin was given intramuscularly and repeated on the 3 following days. On the 3rd day, the patient rested and slept fairly comfortably. He was still incontinent of urine. Muscular rigidity continued to be marked. The rectal temperature varied from 99.8 to 101°F.

During the next 4 days, there was steady improvement. Trismus and muscle spasticity decreased, there were fewer severe muscular contractions, and the patient was able to speak and smile more normally. On the 7th day, however, the patient vomited a small amount of yellow-green material. The vomiting continued despite sedation and on the 8th day became projectile. All oral medications were vomited, and the patient became extremely restless. The temperature had risen to 104.6°F, the pulse to 136, and the respirations to 36. One thousand cubic centimeters of normal saline solution was given by clysis. Later in the day the rectal temperature rose to 106.6°F. Penicillin in doses of 10,000 units every 3 hours was given intramuscularly.

On the 9th day, a surgical consultant examined the patient because of abdominal pain and moderate distention, but believed that there was no intra-abdominal disease. Later in the day the temperature dropped to 102.6°F. The pulse was 128, and the respirations 30. Projectile vomiting continued and became more violent. The red-cell count was 6,380,000 and the white-cell count 15,400, with a moderate shift to the left in neutrophils—probable evidence of hemoconcentration and dehydration, a factor to be considered in the light of vomiting and perspiration. The hemoglobin was 15.3 gm.

On the 10th day, oxygen was started. Blood examination showed correction of the hemoconcentration. The red-cell count was 4,760,000. Urinalysis showed many hyaline and granular casts but was otherwise negative. A second lumbar puncture was performed. The dynamics of the spinal fluid could not be ascertained because of difficulty in controlling the patient. The fluid contained 26 red cells and 1 lymphocyte per cubic millimeter. Pandey's reaction was negative. No organisms were seen in the smear of the fluid. The protein was 25 mg. per 100 cc. Culture showed no growth.

Projectile vomiting continued, and terminally the vomitus contained a large amount of greenish-black material of foul

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odor, which was partly aspirated into the lungs. Artificial respiration and dependent drainage were of no avail, and the patient expired.

Autopsy (performed by Dr S M Brooks) The body was that of a moderately emaciated child. There was a healing scar at the site of the excision of the original infection. The bronchi contained green-brown gastric material, and there were a few areas of red-brown mottling on the cut surfaces of the lungs. The stomach was somewhat dilated and contained thick, greenish-brown fluid. The urinary bladder was empty.

The dura of the brain was of normal thickness and appearance and was not adherent to the calvarium. The right lateral sinus contained an ante-mortem thrombus extending into the superior sagittal sinus and the jugular vein. The thrombus was not adherent to the walls of the sinus and the intimal lining of the sinus appeared smooth and glistening. The cerebral vessels were not remarkable. The convolutions of the brain were slightly flattened, and there was slight narrowing of the sulci. The brain weighed 1360 gm — approximately 10 per cent more than normal for this age. Coronal sections showed a slight pink tinge in some places in the white matter, and the nuclei of the brain stem and medulla were pinker than normal. The petrous and mastoid bones and accessory nasal sinuses were not remarkable. The spinal cord did not appear grossly abnormal except for a slight pinkness of the cut surfaces of the anterior horns in the cervical and lumbar enlargements. A blood culture showed no growth in 9 days. Other tissues and organs showed no lesions.

Microscopical examination of the thrombi from the dural sinuses revealed a few organizing fibroblasts. The dura was not inflamed, and the thrombi were not adherent. The pulmonary alveoli contained gastric contents, and there were small hemorrhagic areas throughout the lungs. The basal ganglia and midbrain nuclei showed dilated blood vessels. The excised wound showed new fibrous tissue deep in the wound and close to a nerve bundle, but there was no foreign material or foreign-body giant cells about the wound. Other tissues showed no histologic lesions.

According to Pratt's¹ method of rating, this case may be considered one of moderately severe tetanus infection. In retrospect it is thought that closer attention should have been paid to hydration and dietary status, in view of the extremely warm weather and the patient's perspiration. The dural sinus thrombosis may well have been the result of dehydration, as shown by Bailey and Hass.² It might have been well to have given half the initial dose of 40,000 units of antitoxin intravenously to fix rapidly any circulating toxin, but the total dose was adequate according to Pratt,¹ although inadequate according to Vinnard.³ Penicillin might have been given earlier and in greater doses with good effect.^{4, 5}

This case demonstrates the advisability of active immunization against tetanus infection early in childhood. It also shows the necessity for early and complete débridement of wounds likely to harbor tetanus bacilli and the wisdom of administering antitoxin in adequate amounts soon after injury in nonimmunized persons.

The unique feature of this case, the aseptic dural sinus thrombosis, appears to have been the direct cause of death. According to Bailey and Hass,² few patients survive this condition, and autopsy of survivors shows severe brain damage. In 52 per cent of the 80 cases reported by these authors, the dural sinus thrombi were septic. All the patients with nonseptic dural sinus thrombi were less than thirty months old, and the average age was nine months. As a rule a period of extreme hyperthermia precedes death. The patient in the case reported herein was six years old and had a rectal temperature of 106.6°F three days before death.

Neurologic signs in these cases are diverse and undependable. The spinal fluid may or may not be under increased pressure, it is usually xanthochromic and contains 10 to 1000 red cells per cubic millimeter. Tests for increased globulin are generally positive, the sugar level is normal.

The terminal findings in this case may be correlated with the dural sinus thrombosis, which probably began to form on the seventh hospital day.

SUMMARY

A case of tetanus in which death was probably due to an aseptic dural sinus thrombosis is reported, and certain of the unusual findings are discussed.

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MEDICAL PROGRESS

PULMONARY TUBERCULOSIS

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ALTHOUGH a voluminous literature covering the field of pulmonary tuberculosis has appeared during the last year, few outstanding advances have been made. Many papers, however, deserve mention because of their help in the diagnosis and treatment of the disease.

CONTROL AND CASE FINDING

In the last few years, since the advent of the miniature roentgenogram, case finding has achieved an unprecedented popularity. Fortified by public funds, the United States Public Health Service and other agencies are now well in the midst of programs to search for tuberculosis in every nook and cranny in this country. As a result, the number of known cases of tuberculosis has increased, but facilities for their care in sanatoriums have not expanded at a comparable rate. This lag in accommodations is noted and lamented in many recent publications.

Hilleboe¹ estimates that at the end of 1945 about 20,000,000 persons in the United States aged twenty years or older (1 in every 5 adults) had chest roentgenograms taken by the armed forces, health departments, industrial firms or voluntary agencies. But case finding is only one step in the control of tuberculosis, isolation and treatment are equally important. Patients with cases of active tuberculosis must be given medical care and must be isolated to prevent further spread of the disease. Hilleboe points out that there is a lack of vision in case finding if treatment is delayed by a shortage of sanatorium beds, adding "In every industrial community in which a tuberculosis control campaign is undertaken, plans must be made for the provision of a sufficient number of beds. Temporary facilities may, for a time, be utilized until the people, realizing the seriousness of the community's plight, will demand the construction and maintenance of the necessary hospitals."

Elsewhere, Hilleboe and Gillespie² phrase this same thought somewhat differently:

Unfortunately, after a physician has made a diagnosis of active pulmonary tuberculosis and has recommended sanatorium care, it may be found that sanatorium beds are not available. Therefore, it is necessary for physicians to care for these patients at home. This means that the physician must employ techniques used in the modern sanatorium including bed rest, nursing care, isolation, precautions, and general and personal hygiene.

If a physician keeps a patient close to the sanatorium routine at home while awaiting admission to a sanatorium, he is frequently surprised, at least in my experience, at the progress the patient exhibits in a short time.

The trend of the times in case finding is further illustrated by statistics from the State of New York, where Mikol and Plunkett³ report that from 1924 through 1939 in men, and from 1924 to 1941 in women, there was an almost steady decline in the annual number of cases of respiratory tuberculosis. Among the former a striking reversal of this trend began in 1940, reaching a peak in 1942, during which the number of cases was 38 per cent higher than in 1941. This increase was largely due to an increase in the minimal cases in the age group from twenty to thirty-four years. Mikol and Plunkett believe that this increase is due to the discovery of more cases by the various mass surveys rather than to any actual increase in the development of new cases. The greater incidence of pulmonary tuberculosis in young men and women is probably more apparent than real.

The extent to which case finding and hospitalization of discovered cases will eventually lower the tuberculosis death rate is not known. Nor are there reliable data regarding the number of early cases that will reactivate in spite of prompt hospitalization. Nevertheless, the tuberculosis mortality rate continues to show a gratifying decline. In the United States in 1944 it was at its lowest figure 41.3 per 100,000 population, as compared with 42.6 in 1943 and 43.1 in 1942. In Massachusetts, the death rate in 1944 was 40.8, as compared with 42.7 in 1943. According to preliminary estimates for 1945, the number of deaths from tuberculosis has continued to decline, but no exact figures are available. It must be pointed out, however, that statistics collected during the war years are not wholly reliable because of both the large shift of population groups and the considerable number of the population that has been overseas.⁴

Tuberculosis in Persons over Fifty

Myers⁵ points out that tuberculosis mortality is higher among Americans after the age of fifty years than at any other time in life, and that this fact is apparently not generally recognized, as indicated by the belief that human beings rarely have tuberculosis in the later decades of life. Since the average

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age of the population is increasing, the number of cases of tuberculosis in the aged is showing a commensurate rise. Besides, the disease in the elderly may be even more prevalent than mortality statistics suggest, since a significant number of deaths are not accurately reported. Myers cites the case of a man who had had a cough and a positive sputum for thirty years and who had presumably infected two daughters. At the age of eighty-two this man spent the winter in another state, where he became acutely ill and died within twenty-four hours. The local physician had no opportunity to examine him adequately. On the death certificate the cause of death was stated as "coronary disease," and no mention was made of tuberculosis.

Although tuberculosis is frequently discovered in elderly persons, Myers cautions that the diagnosis should not be made without adequate evidence. An aged person with a chronic cough and expectoration does not necessarily have pulmonary tuberculosis. Symptoms, signs and x-ray appearance are not pathognomonic. The only absolute diagnostic finding is the presence of tubercle bacilli, confirmed by culture or animal inoculation.

Tuberculosis among Nurses

On the basis of considerable evidence obtained from reviewing the medical literature and from his own experience, Cameron⁶ believes that nurses are exposed to a real hazard while caring for tuberculous patients. He emphasizes that nothing is gained by minimizing the facilities for tuberculous infection that exist in a sanatorium. Reported statistics indicate that the incidence of tuberculosis among nurses varies from 1.6 to 6 per cent, with a probable average of about 3 per cent. Yet, surprisingly, practically all superintendents of sanatoriums agree that tuberculous disease among their staffs is rare. The reason for this apparent contradiction, Cameron points out, lies in the fact that there is no follow-up of those employees who have left the institutions. Another possible reason is that many nurses are covered by the blanket classification "housewife" in hospital statistics and reports. Actually there are many registered nurses, attendant nurses and various ward helpers whose occupation at the time of admission to the sanatorium is "housewife" and whose earlier employment and possible infection are ignored.

Statistics regarding tuberculosis among nurses are probably much too low. Cameron observes that the repeated infections to which nurses are exposed are an undoubted risk. The greatest danger, of course, lies in young girls whose reactions to the Mantoux test are originally negative, although there is theoretical danger even to those whose reactions are positive. Cameron carries this thesis still farther, pointing out that to control tuberculosis among nurses working in sanatoriums the administrators

should concern themselves with the mental and spiritual well-being, as well as the physical status, of the employees. He writes as follows:

An emancipated spirit fortifies a well-tended body, and strength of body and serenity of mind are the best defences against tuberculous invasion. The living and working conditions of tuberculosis nursing must be good. Mental freedom is just as important as physical well-being.

It is my belief that if more sanatorium administrators placed greater value on the wisdom of these words, there would be far less of a nursing shortage in many institutions.

Tuberculosis in Repatriated Prisoners

Brooke⁷ provides a partial answer to the question of the extent of tuberculous involvement in repatriated prisoners of war. Of course, his figures are not wholly adequate in that they do not include patients who died in prison camps because of the disease. Of 1507 prisoners repatriated from Japanese camps he found that 118 (7.8 per cent) had active or questionably active pleural or pulmonary disease. Of these, 24 were believed to be questionably minimal, and 33 minimally active. Repatriated prisoners had a lower incidence than had been anticipated.

Tuberculous Families and Household Associates

Many workers have speculated on the factors that control the incidence of clinical tuberculosis in a given household. It is a frequent clinical experience that not every person in a household develops active tuberculosis even when the extent of the exposure to an open case is roughly comparable in all the members of the household unit. To determine the reasons for this variability, Puffer and her associates⁸ investigated family contacts in Williamson County, Tennessee. Careful studies of the associates of 519 white and 111 colored index cases revealed that the prevalence among white associates increased from a low rate in persons under fifteen years of age to a high rate for those thirty-five years and over. The incidence among colored associates did not show this distribution; relatively high rates were found in all age groups. In white associates thirty-five years of age or older 12.9 per cent of the blood relations had manifest tuberculosis, whereas only 7.4 per cent of those not related had the disease. In the age group fifteen to thirty-four years the attack rate for white household associates related by blood was 0.8 per cent, and for those not related it was 0.3 per cent. Obviously, blood relatives show a greater attack rate and a greater prevalence rate than those not related.

These data are supplemented by the report of Telford and Garten-White,⁹ of the Los Angeles County Health Department. Whereas they had been inclined to discount the lay conception that there is a familial susceptibility or resistance to the disease,

they are forced to conclude that there may be some factual or at least statistical basis for this relief. Their figures showed that a comparatively small proportion of the families exposed presented nearly all the new cases, and they believe that the attributes that make these families more than ordinarily susceptible deserve earnest study. If the characteristics of these groups can be recognized, public-health efforts can be devoted more intensively to such families than to the community at large.

It is pointed out that a crowded living condition, although a major contribution to a greater familial incidence of tuberculosis, is not the only factor involved. A survey of patients in 1940, for example, revealed that about 50 per cent of 1637 contacts developed active reinfection tuberculosis six months or more after the discovery of the first known case in each of the families. In 1944, in spite of apparently improved social and economic conditions, the attack rate was found to be insignificantly lower—4.8 per cent. Other surveys conducted at the same time in congested areas yielded an attack rate of only 0.5 per cent. The great hazard in families with a high attack rate is apparently due not only to the direct spread of the infection but also to other factors and conditions favoring the spread. Telford and Garten-White therefore believe that some inherent fault in either physical or mental make-up makes the members of such families more susceptible than the average person, or that contributory domestic habits have not been overcome by the usual public-health education and supervision. They write as follows: "Isolation of active cases of tuberculosis, either outside the home or in the home with intensive supervision, should be stressed in proportion to the number of cases in the family or to cases known in the recent family history."

On the basis of these detailed investigations one can reasonably conclude that it takes more than mere contact with the tubercle bacillus to develop clinical disease. The factor of familial susceptibility must be considered in the management and prognosis in any given case. Further elucidation of the factors of familial susceptibility is certainly indicated.

ANATOMICAL CONSIDERATIONS

Since bronchoscopy and surgery are playing such an important role in the diagnosis and treatment of pulmonary disorders, a wider understanding of the segmental anatomy of the tracheobronchial tree is essential. Localization of a pulmonary lesion in relation to its appropriate bronchopulmonary segment often helps clarify the nature of a suspicious roentgenologic shadow, and may provide a clue to its proper management. No longer can it be considered adequate to describe a "spot" as being at "the level of the third anterior interspace." In the following three studies¹⁰⁻¹² one can obtain the essentials for a more complete understanding of the tracheobronchial tree and its pulmonary segments

as viewed by the anatomist, the bronchoscopist and the roentgenologist.

The anatomist's point of view is presented by Boyd¹⁰ in a series of excellent dissections and exquisite colored plates. Briefly, some of the significant facts are as follows:

Right bronchial tree. The upper or *superior-lobe bronchus*, which arises almost at the bifurcation of the trachea, is very short, branching almost immediately into three stems—the apical, anterior and posterior segmental branches. The apical segmental branch divides into anterior and posterior rami. The anterior one divides into a lateral ramus going to the axilla and an anterior ramus descending to the inferior portion of the upper lobe. The posterior segmental branch divides into a posterior ramus, with its posteriorly placed orifice and its predilection to abscess, and a lateral ramus. The *middle-lobe bronchus* divides into a medial and a lateral segmental bronchus, which show considerable anatomic variation, and there is some shifting from one segment to another. For this reason resection of either the medial or lateral segment is technically difficult, and if operation is indicated both segments are usually resected together. The *lower-lobe bronchus* divides first into a superior segmental bronchus, which has a posterior horizontal distribution and, surgically, can be readily identified and removed separately. Between the superior bronchus and the remaining segmental bronchi of the right lower lobe there is an interval of 1.5 cm., which is the common stem of the four segmental bronchi that reach to the base or the diaphragmatic surface of the lung.

Left bronchial tree. The upper or *superior-lobe bronchus*, which originates farther down on the left side than on the right, arises from the anterolateral instead of the posterolateral surface of the main bronchus. It divides into a superior and a lower (or lingular) division. The upper division gives off an apical posterior segment and an anterior (or pectoral) segment. The lower or lingular division has superior and inferior segments, the lingula being analogous to the middle lobe on the right. The inferior or *lower-lobe bronchus* gives off several segmental branches that are designated as superior, anteromedial basal, lateral basal, and posterior basal. As on the right, the superior segment has its orifice posteriorly, close to the point of origin of the bronchus itself. The basal segments on the left differ from those on the right in that they are three in number instead of four and usually branch by trifurcation rather than by bifurcation.

Hagens¹¹ dissected the lungs of 20 cadavers to clarify the appearance of the bronchial tree from the standpoint of the bronchoscopist. He was thus able to map out the various orifices that are such important landmarks, to determine their diameters and to make many measurements to establish their usual relations. This paper should be read in conjunction with that of Boyd,¹⁰ since the data and descriptions tend to supplement each other.

Clarification of the anatomic arrangement of the tracheobronchial tree makes more readily understandable the valuable series of articles by Robbins and his associates¹²⁻¹⁴ on the roentgenologic appearance of the segmental collapse of the lung. These investigators recommend that when pulmonary disease is suspected the patient be studied fluoroscopically and that in addition he have a routine posteroanterior film, a lateral film and an anteroposterior Bucky or Swedish-grid roentgenogram. With these few studies approximately 80 per cent of patients with pulmonary disease need no further roentgenologic investigation to establish the diagnosis. The usual diagnostic criteria of segmental

collapse of the lung, Robbins et al point out, are an abnormal shadow of increased density, elevation of the diaphragm, displacement or shift of the mediastinum and narrowing of the rib spaces. After a detailed analysis of 1200 cases of tumor, bronchiectasis, foreign body and tuberculosis, they were able to add three more criteria to this original list: the appearance and position of the hilar shadows, the arrangement of the vascular shadows and the demonstration of the actual size of a lobe as determined by the appearance and position of the septums or fissures of the lung. Displacement of a hilus upward, for example, indicates possible collapse of an upper lobe.

Although collapse of an entire lung or a major portion thereof is usually readily recognizable from established criteria, segmental collapse may be more difficult to identify. Collapse of a lower lobe occurs rather frequently but is often overlooked or misinterpreted because the shadow of increased density is small and so located that it is hidden by overlying structures, such as the spine, diaphragm and mediastinum. Usually the first sign of collapse of a lower lobe is a posterior displacement of the interlobar septum. Lung markings of the collapsed lobe later become crowded together. If the collapse is confined to the dorsal division of the lower lobe it may be identified as a triangular area of density and by the sharp angulation of the posterior portion of the major interlobar septum. Since bronchiectasis usually spares the dorsal division, whereas tuberculosis and lung abscess are often found in that area, accurate localization of the collapse is frequently an aid in differential diagnosis.

Collapse of the right middle lobe of the lung also occurs frequently but is often confused with interlobar effusion. Complete obstruction of the bronchus to the right middle lobe causes the lobe to decrease in size and assume a pyramidal shape, with the base against the right border of the heart and the apex extending toward the lateral chest wall. The result is a loss of definition of the right border of the heart. In this event the lateral view is the most important single factor in the examination, and its appearance may be deceptively like that of a pleural effusion. A lordotic view may help further in the differentiation of these two conditions.

Collapse of a single lobe of a lung is most frequently misinterpreted in one of the upper lobes, where it is confused with a localized area of consolidation, a mediastinal tumor or an aortic aneurysm. In some cases it may be completely overlooked. One of the first signs of collapse of an upper lobe is displacement of the major septum anteriorly and superiorly as determined in the lateral film. Careful attention to detail on all the x-ray films is essential to accurate diagnosis of collapse and to differentiation from other pathologic conditions.

An understanding of the bronchial pattern also helps in an evaluation of the status of a bronchus

that drains a tuberculous cavity. According to Camiel,¹⁴ the roentgenologic appearance of the lung in the area between a tuberculous cavity (or the site of a previous cavity) and the hilus is of special importance. This portion of the lung contains the regional bronchi and the peribronchial vascular and lymphatic channels that drain the area of the parenchymal lesion toward the lung root. These draining bronchi, which are frequently involved in the tuberculous process, can often be visualized roentgenologically, and their appearance depends on the severity and duration of the underlying process or disease. Bronchial thickening due to edema or thickening resulting from extension of the disease into the bronchus with subsequent fibrosis increases the visibility of the bronchial shadow and thus makes possible a diagnosis of endobronchial tuberculosis.

BRONCHOSPIROMETRY

With the greater interest in the detailed anatomy of the bronchial tree during the last few years there has been a corresponding interest in greater refinements of technic for determining the functional capacity of the lungs. In many cases it is no longer adequate to make one determination of a patient's vital capacity in the belief that it provides a reliable gauge of his pulmonary function. The vital capacity can be considered rather as a rough guide that fails to disclose any information concerning the function of each lung and therefore may be misleading.

Bronchspirometry, on the other hand, provides the additional data that are often lacking. With this procedure it is possible to make many different determinations on each lung (such as tidal air, respiratory rate and vital capacity) and to decide what functional share each lung is contributing to the total. Some of the significant facts that can be learned from bronchspirometric studies have been recently reviewed by Pinner, Lein^{er} and Zavod,¹⁵ who found that bronchspirometry often revealed decreased function in one lung when regular spirometric studies were normal or nearly normal. For example, they cite the case of a twenty-nine-year-old man with right pneumothorax, whose vital capacity on spirometry was 2650 cc. Maximum breathing capacity divided by minute volume was 11.3, a finding consistent with a normal respiratory reserve. Yet on bronchspirometry the oxygen intake of the right lung was discovered to be only about a third of the total oxygen intake in spite of a normal respiratory reserve; the right lung contributed only about 30 per cent of the total oxygen intake instead of its normal contribution of 54 per cent.

One of the most valuable findings resulting from these bronchspirometric investigations is the demonstration that a marked discrepancy may exist between the clinical findings, the x-ray appearance and the actual function of the lung. Cases are cited

to show that a slight amount of fibrosis (as determined by x-ray study) may be accompanied by a considerable amount of functional damage. Conversely, in a lung that appears on x-ray examination to be heavily infiltrated or even riddled by cavities, the impairment in function is hardly appreciable. Curiously enough, when special studies were made on patients whose lung function was extremely poor, it was found that practically all these patients had either obliterative pleuritis or phrenic paralysis. Pinner et al. emphasize the fact that pleural involvement that cannot always be diagnosed by roentgenologic examination may lead to severer functional damage than a more obvious parenchymal lesion.

Collapse therapy (pneumothorax) causes a reduction in the oxygen intake of the collapsed lung. Compensation for this decrease is accomplished by both a commensurate increase in the contralateral lung and a cardiovascular factor. The respiratory burden on the contralateral lung is considerably less than one might anticipate. It therefore follows that if a patient with unilateral pneumothorax is dyspneic at rest, the cause is not likely to be found in the extent of his collapse but rather in a possible functional impairment of the contralateral lung. That therapeutic pneumothorax (or the disease itself) may leave the lung with permanent functional disability is demonstrated by the fact that re-expanded lungs show some degree of respiratory impairment. Twenty-six cases of thoracoplasty studied showed surprisingly less diminution in pulmonary function than those treated by pneumothorax. But, as Pinner and his colleagues¹⁵ point out, more cases will have to be explored by this method before it can be certain that the differences detected are not merely the results of random sampling. An interesting side light brought out by bronchspirometric investigation is that immobilization by sandbags or by strapping with adhesive does not achieve a reduction in the ventilation or the respiratory work of the underlying lung.

Tests of pulmonary function, in a way, are analogous to those of renal function. In diffuse bilateral disease, the total function (as determined by routine spirometry) may provide all the data that the clinician needs. On the other hand, in unilateral disease or in predominantly unilateral disease or when surgery is contemplated, data regarding the function of each lung separately may provide invaluable information.

BED REST

The recent discussions covering strict bed rest as a method of treatment have stimulated renewed interest in this type of therapy for tuberculosis. Obviously, strict bed rest is not without its limitations and contraindications in tuberculosis as in many other ailments. Peck¹⁶ described the progress of a group of patients at the Detroit Municipal Tubercu-

culosis Sanatorium who were placed on a regime of bed rest with instructions never to sit up, never to raise the head from the pillow and to lie as inertly as possible. Difficulties soon began to appear. Cough frequently increased, with roentgenologic evidence indicating poor drainage of secretions, and a few patients showed serious extension of the disease. Many complained of increased nervousness and fatigue. Peck concluded that strict bed rest may at times be harmful and may actually defeat the purpose for which it is given.

It was recognized soon after this experiment that rest in the supine position violated a well established surgical tenet — that drainage from abscess cavities must be free and adequate. Since most tuberculous cavities are posteriorly placed, such a position interferes with drainage, makes the cavity dependent, encourages toxicity and enhances spread. Because of these considerations, the regime at the Detroit Municipal Sanatorium was modified to allow the patient reasonable motion in bed, adequate drainage of cavities, relief from bronchial spasm and liquefaction of sputum by means of steam inhalations. The problems of muscular relaxation and mental repose — a much neglected aspect of treatment in the routine management of sanatorium cases — were also given consideration.

This new regime of treatment was then applied to 69 patients, most of whom had extensive bilateral disease and cavitation. Of these, 19 had cavity closure with conversion of sputum, 14 responded favorably enough to permit thoracoplasty, 26 were studied for an insufficient length of time, and 10 died. In a control group of cases (the difficulties in finding true controls are admitted), selected because of similar age and comparable lesions by roentgenogram, only 2 patients had cavity closure and sputum conversion, 7 progressed to thoracoplasty, 12 were discharged improved, and 48 died. In Peck's opinion carefully supervised bed rest is effective therapy, giving results entirely commensurate with the time and energy involved.

Elsewhere, Peck and Willis¹⁷ direct criticism to so-called "postural rest," in which patients with unilateral cavitation are encouraged to lie on the cavity side with the idea that the uninvolved lung will be protected from positive sputum. They believe, with good reason, that such an argument is fallacious and that postural rest cannot maintain unilateral sepsis. They cite the case of a thirteen-year-old girl who had been kept on one side for three months, with consequent bathing and saturation of the dependent lung in its own secretions. Examination showed that this girl had extensive bronchiectasis of the upper lobe of the dependent lung, which may well have developed as a direct result of improper bed rest. No physician would give the same dose of insulin to all his diabetic patients, and yet the same dose and same type of bed rest is prescribed for all tuberculous patients in some sanatoriums.

This condemnation of strict bed rest for all patients is carried still farther by Brav,¹⁸ of the New York State Hospital for Incipient Tuberculosis, who points out that few published reports substantiate the alleged value of strict bed rest for tuberculous patients who are in a good nutritive condition and entirely or practically free from symptoms. Contrary to some expressed opinions, early tuberculous lesions, especially those in the upper part of the lung, have a marked tendency to heal and are usually not progressive. This point is readily demonstrated in Brav's studies of 67 cases, whose lesions were less than a year old as determined by serial roentgenograms. In no case did the patient receive strict bed rest, all were ambulant from the time the disease was discovered, throughout their sanatorium stay and subsequently, for a period averaging thirty months. The results were favorable in 57 (85 per cent of these cases). Although the number of cases was too small for definite conclusions, this experience is comparable to the best statistics obtained with strict bed rest. Bed rest, like any other form of therapy, should be individualized both in the early and in advanced cases.

An ingenious but still unproved theory advanced by Dock¹⁹ to account for the apical localization of pulmonary tuberculosis has some bearing on bed rest. Dock points out that in man the mean pulmonary arterial pressure is equivalent to 15 to 18 mm of mercury, which, in turn, is equivalent to a column of blood 12 to 23 cm in height. Since the apex of the lung is 15 to 30 cm cephalad to the right ventricle, the pulmonary arterial pressure in the upper 5 cm of the lung, even in systole, is at most equivalent to 10 mm of mercury. Because a pressure equivalent to about 15 mm. of mercury is required to overcome the difference in colloidal osmotic pressure between the plasma and the pulmonary tissue fluid, it is likely that no lymph is produced in most adults while they are in the erect posture. As a result, it is claimed, few lymph-borne and cellular antibodies reach the apical portions of the lung while a person is sitting or standing.

But Dock affirms that this fact does not mean that a person with tuberculosis must lie flat on his back all the time, it simply means that if he is taking bed-rest treatment he should be recumbent and not sitting up. At least part of the day should be devoted to recumbency to overcome the hydrostatic pressure within the pulmonary circuit. Dock's conclusion is as follows:

It is quite possible that if the patient were allowed up, when he felt strong enough, for ten to thirty minutes four or five times a day, his moral and physical strength would be better preserved or more quickly restored. Even if this were permitted in the mornings, when the afternoon temperatures were elevated, it might do more good than harm.

Such a program might enable a patient to accept recumbency as a therapeutic measure with a greater

degree of physical and mental ease and might thus make the entire treatment more effective.

PLEURISY WITH EFFUSION

It is becoming increasingly evident that pleurisy with effusion, especially in young adults, most frequently has a tuberculous etiology. Farber's²⁰ recent follow-up studies clearly demonstrated that a significant number of patients with pleural effusion develop pulmonary tuberculosis. Of 111 patients followed for three years or longer, 38 (34 per cent) developed parenchymal disease, and 27 died. This indicates that the prognosis in cases of pleurisy with effusion should be guarded.

More recent investigations are consistent with this point of view. For example, Bird's²¹ evaluation of the clinical course of 7 cases of alternating pleurisy with effusion in patients between the ages of twenty-one and thirty-six, with an average age of thirty-two, demonstrated a tuberculous background in all but 1. In several cases, tubercle bacilli were found on culture or guinea-pig inoculation when direct smears were reported as being negative. It must be stressed that the more delicate the test, the greater the likelihood of recovering the tubercle bacillus. Close²² also found that as the bacteriologic technic improved, the number of proved positive cases increased from an average of 40 per cent to one of 70 per cent. In his most recent series of cases, among 159 young adults hospitalized for pleural effusion he recovered tubercle bacilli by culture on the Lowenstein-Jensen medium in 90 per cent of the cases in which the diagnosis of tuberculosis was eventually made on clinical grounds. He states: "No opportunity for culturing should be neglected. Even 1-2 cc of what looks like blood from an unsuccessful attempt at aspiration should be put on culture medium. From three such lung punctures tubercle bacilli have been obtained."

Similarly, Feldman and Lewis²³ are of the opinion that bacteriologically sterile effusions carry the same import as those that are positive, active caseous tuberculosis being directly responsible for the onset of the effusion even when the fluid remains sterile. At the Rhoads General Hospital they thoroughly investigated 59 patients with pleural effusion, especially for the presence of tuberculosis. The fluid was on the right side in 39 cases, on the left in 18 and bilateral in 2. The onset of the disease was described as "insidious" in 34 cases, "acute following a prodrome" in 18, and "acute, fulminating" in 9. In 2 cases with insidious onset, the patient developed a fresh pleural effusion on the opposite side after the original one had subsided, both cases had suggestive parenchymal infiltration and hilar enlargement. Feldman and Lewis conclude that pleural effusion occurring in young persons in whom no other readily demonstrable cause exists can be considered tuberculous until clearly proved otherwise.

Since tuberculosis figures so significantly in the etiology of pleurisy with effusion it is essential that these patients be followed, like any tuberculous person, by frequent check-up and x-ray examinations. Feldman and Lewis recommend such a follow-up to extend for five years after the onset of the effusion, with special emphasis on the first year. For therapy, they advise complete evacuation of the chest (in stages, if necessary) and the introduction of 200 to 300 cc of air into the pleural cavity to obtain better x-ray visualization of the lung parenchyma. It seems logical that if tuberculosis is suspected, the contacts of all patients with pleurisy and effusion should be investigated to determine the possible source of the infection.

CHEMOTHERAPY AND ANTIBIOTICS

Streptomycin

Each year some new therapeutic weapon seems to offer the victims of tuberculosis a quick and dramatic rescue from their long and costly illness. This year the "hope on the horizon" is streptomycin. Although its precise indications and limitations have not been worked out in human tuberculosis, there can be no question about its effectiveness in animals. Injected into guinea pigs, streptomycin was found to exert a striking inhibitory action on the activities of *Mycobacterium tuberculosis* in vivo but did not succeed in eliminating or killing all the bacilli in the animals.²⁴ In mice, whose resistance to tuberculosis is greater than that of guinea pigs, a comparable effect was noted, and the suppressive action was characterized as marked even though the tuberculous infection was not completely suppressed.²⁵ After a more extensive and better controlled series of experiments, Hinshaw and Feldman²⁶ reported that streptomycin appeared to be more effective than any of the sulfonamide drugs and much less toxic for guinea pigs.

Under the direction of Hinshaw and Feldman²⁶ streptomycin therapy for human tuberculosis was begun in December, 1944. At first, small ineffective doses were used, with inconclusive results. With further knowledge of the pharmacologic properties of the drug, it was soon established that the minimal daily dosage should be 800,000 "S" units (1000 "S" units equal 1 mg of streptomycin), and usually the patients received from 1,000,000 to 2,000,000 units by intramuscular injection at three-hour intervals. No serious toxic effects were noted, but in 4 cases sensitization to the drug was apparent, so that violent febrile reactions developed when the drug was administered after an interval of a few weeks. In some cases transient deafness and disturbance of vestibular function were observed, but it is not known whether this was due to the streptomycin or to some impurity. At any rate, of the 16 patients treated for one to three months, no rapid curative action was seen. Lesions that were soft and of known recent

origin tended to improve promptly, but in some cases there was reactivation when the drug was discontinued. All that could be said for streptomycin was that it had a limited suppressive effect.

Subsequently, in a more detailed report, Hinshaw and Feldman²⁷ cited their experience with 54 patients with tuberculosis who had received streptomycin treatment for periods of more than four weeks. In each case the disease had shown a tendency toward unfavorable progression prior to the institution of therapy. In 21 cases the patients had pulmonary tuberculosis, which in 16 was far advanced with the addition of infiltrations of recent origin. Of the 21 pulmonary cases studied, objective evidence of improvement was observed in 16. An antibacterial action was not noted, but a suppressive effect was found so long as administration of the drug was continued. Streptomycin was also used in cases in which there were tuberculous sinuses, but in 3 of 5 cases the sinuses recurred after the drug was discontinued. In tuberculous empyema and in urogenital tuberculosis the results must still be regarded as inconclusive.

Supplementing this report by Hinshaw and Feldman, Cooke and his colleagues,²⁸ at the Yale University School of Medicine, recorded the recovery of a child with tuberculous meningitis. The infant was admitted to the New Haven Hospital on May 12, 1945, with convulsions, and the diagnosis of tuberculous meningitis was incontrovertibly established. Streptomycin was begun seven days later and continued for thirty days. Therapy was discontinued because of lack of the drug, but was resumed on July 9 for an additional twenty-nine days. At the time the report was written (December 31, 1945) the child was still alive and apparently improving, although there were some residual neurologic impairment, cervical adenopathy and abnormal pulmonary findings. Acid-fast bacilli had not reappeared in the spinal fluid, however.

Other Antibiotics

The *Bacillus subtilis* produces a substance called "subtilin" that has a bacteriostatic action in vitro against the tubercle bacillus in high dilution (1:100,000) and appears to be germicidal in greater concentration (1:50,000).²⁹

Mattick and Hirsch³⁰ isolated a streptococcus that destroys tubercle bacilli in vitro. On exploring the widely held notion that the acid in sour milk had a destructive action on tubercle bacilli, they found that it was not the acid per se or the lactic streptococcus that was responsible for the tuberculocidal action of sour milk, but another streptococcus — "the inhibitory streptococcus." This organism, they claim, produces sufficient antibiotic substance to kill or render avirulent up to 2000 tubercle bacilli per cubic centimeter of milk. These tests, which are preliminary, await confirmation.

Chemicals

Clinical interest in the sulfonamides is waning — perhaps rightly so. Their value in clinical tuberculosis is less than the earlier results seemed to indicate. For example, at the Firland Sanatorium in Seattle, diasone was given to a group of 10 patients for one hundred and nineteen days without any appreciable alteration in the course of the disease as compared with a group of controls.³¹ Neither the sputum nor the x-ray findings showed any benefit. Similarly, at the Chicago Municipal Tuberculosis Sanatorium, Tice and his co-workers³² failed to note any improvement when the therapy was adequately controlled. In their tests, 29 patients with far-advanced tuberculosis were given diasone, but only 16 completed the course of therapy for one reason or another. After six months the results in the diasone-treated patients and in the controls ran parallel. Five of the former and 4 of the latter improved, whereas there were 14 unimproved treated patients and 11 unimproved controls, and 10 dead treated patients and 15 dead controls.

Both the chorioallantoic membrane of the chick embryo and the anterior chamber of the guinea pig's eye have been found to serve efficiently in the evaluation of new drugs for their possible bacteriostatic action. Thus, Steenken and his colleagues³³ showed that ocular tuberculosis in the guinea pig could be fairly well controlled and retarded in its progress by both the oral administration and the local instillation of promin. The method of eye infection offered a relatively rapid and easily observable method of testing new chemotherapeutic agents for the treatment of tuberculosis.

Twelve different alicyclic acids — chemically related to chaulmoogra oil — were tested by Emmart³⁴ in vitro and four were also studied in vivo (chick embryo) for tuberculostatic action. Four cyclopentyl and cyclohexyl compounds were found to be highly tuberculostatic in relatively low dosage. Emmart believes that further animal studies with these chemicals will prove profitable.

MISCELLANEOUS TOPICS

Amyloid Disease

Chronic suppuration, tuberculous or otherwise, usually leads to amyloid disease, which is almost universally regarded as having a poor prognosis, although the interval between the onset of symptoms and death varies considerably from patient to patient. Jacobi and Grayzel³⁵ recently directed attention to the therapeutic benefits of liver for such patients. In their series of 69 cases all the nontreated patients died, whereas 9 of the 16 treated patients were definitely cured and 3 others showed clinical improvement or prolongation of life. They recommend that in addition to intensive treatment of the primary infection, the patient be given 2 to 8 gm of desiccated powdered whole liver three times daily. Since not all liver preparations are comparable in

their potency against amyloid disease and since the treatment is long and costly, fresh liver may be prepared according to directions given by the authors.

The relation between amyloid disease and the necessity for surgical treatment often creates perplexing problems. To determine whether patients with amyloid disease are benefited or harmed by surgery, Auerbach and Stemmermann³⁶ analyzed the records of 486 cases of amyloid disease in which the diagnosis was proved by autopsy. Forty-three patients had fifty-two major surgical operations after the detection of amyloid disease, and 43 had seventy-seven operations prior to the development of this complication. On the basis of these cases, which were comparable in many respects, Auerbach and Stemmermann concluded that the decision to operate is not to be determined by the existence of the amyloid disease itself but by the possibility of controlling the underlying infection. Control of the original infection provides the patient with his best chance for recovery. The presence of amyloidosis should be an added indication rather than a deterrent, according to the authors, who also believe that with evidence of renal or other visceral impairment, surgery becomes obligatory, for although such patients are poor risks, eradication of sinuses and arrest of infection offer the only hope of escaping death.

Tuberculous Laryngitis

Tuberculosis of the larynx is a serious complication of a pulmonary infection and one that is notoriously difficult to treat. According to Humphries³⁷ treatment of tuberculous laryngitis may be regarded as being both medical and surgical. For medical therapy he recommends comforting spray and voice rest. Under surgical treatment he lists galvanocauterization, laryngoscopy, biopsy, nerve block, tracheotomy, arytenoidectomy, bronchoscopy, and collapse therapy. Bronchoscopy is practically never indicated for laryngeal tuberculosis, although it plays an important role in the management of lesions deeper within the bronchial tree. Collapse therapy, by ridding the sputum of tubercle bacilli, has an indirect beneficial action on laryngeal disease. Most satisfactory of all, according to Humphries, is electrocauterization, which gave marked relief in over 90 per cent of his cases.

Myerson³⁸ has advanced the hypothesis that it is not the ulceration of the larynx that is responsible for the patient's pain but the secondary infection of the involved tissues by pyogenic organisms. In support of this point of view he calls attention to the fact that spraying the diseased tissues with sulfanilamide powder brings immediate relief from pain. In his treatments a powder atomizer is used to spray between 0.3 and 0.6 gm of sulfanilamide into the larynx at each application. He has treated 60 patients in this way, with encouraging results. In 14 cases a hopeless condition became favorable following institution of therapy.

Gastric Juice and Tubercle Bacilli

Bacteriologic investigation of gastric juice by culture or by guinea-pig inoculation is often performed in the laboratory examination for tubercle bacilli. Yet there is some evidence that many false-negative reactions may have been obtained because of failure to inject the animals with fresh gastric juice.³⁹ If delay between the time the gastric juice is obtained and its inoculation into an animal is unavoidable, it is best that the specimen be neutralized before being allowed to stand. Three times more positive reactions can be obtained when the specimens are neutralized immediately than after forty-eight hours and nearly twice as many as after a twenty-four hour interval.⁴⁰

Vaccination

Although vaccination against tuberculosis with BCG (*Bacillus Calmette-Guérin*) has never been unanimously accepted, there is increasing evidence that the procedure is of value. This is particularly true in areas where tuberculosis is associated with a high mortality. An impartial evaluation of vaccination with BCG has been summed up in a concise and lucid fashion editorially.⁴¹ In support of the thesis that vaccination provides limited protection to heavily infected groups, the six-year results of Aronson and Palmer⁴² with groups of North American Indians may be cited. This report is based on the study of 1550 vaccinated Indians and 1457 controls who were resident in four widely scattered reservations. The initial testings and vaccinations were concluded in February, 1938, and the cases were followed annually until 1944. These studies showed that there were 60 deaths (from all causes) in the controls, but only 34 in the group vaccinated with BCG. Whereas 4 deaths from tuberculosis were recorded in the vaccinated group, there were 26 in the nonvaccinated. Forty cases of roentgenologically evident disease developed in the group vaccinated with BCG, and 185 cases were detected in the controls. Thus it appears that considerable benefit was obtained by this form of vaccination.

Attention was called in an earlier review⁴³ to the possibility of using the vole bacillus as an immunizing agent against tuberculosis. Present work with guinea pigs indicates that immunization with the vole bacillus takes place but that the degree of protection obtained is apparently no greater than that resulting from vaccination with BCG.⁴⁴

Expectorants

The continuing researches of Boyd and his colleagues⁴⁵⁻⁴⁷ are uncovering many new facts regarding the expectorant drugs. For example, they note that paregoric (camphorated tincture of opium) has been used for many years as a sedative in cough mixtures, with little investigation of its mode of action. But, by measuring the output of respiratory-tract fluid in different animals, they concluded that pare-

goric has considerable expectorant action, and that this action is greater than that of any of the individual components of paregoric or that obtained by a summation of the individual effects. Best results were obtained with preparations that had aged a year or longer. If the afferent vagal nerves from the stomach were severed, paregoric did not augment the respiratory-tract fluid—an indication that it acts reflexly through the stomach.

A variety of volatile oils have also been tested for their ability to stimulate respiratory-tract fluid. Of four terbinthinate oils tested, oil of turpentine proved most effective. Among the other volatile oils, oil of anise was most potent. The authors believe that if these data apply to man they indicate that oil of anise is not being used to its optimal extent as an expectorant drug. The expectorant volatile oils do not act reflexly from the stomach but rather on the secretory cells of the respiratory tract. The inclusion of several different expectorants in one cough mixture does not seem to enhance its expectorant action, as measured by respiratory-tract fluid.

Depth Growth of Bacilli

The growth of bacilli submerged in a liquid culture medium more nearly approximates that of the bacilli in living animal tissues than growth on the surface of a medium exposed directly to the atmosphere.⁴⁸ The technics for obtaining depth growth are described by Drea^{48, 49} who also points out that this type may be used to test the effect of various substances on the growth and nutrition of the tubercle bacillus. By submerged growth technics, Dubos⁵⁰ demonstrated that certain complex lipids had a remarkably stimulating effect on the multiplication of mycobacteria. Addition to Long's synthetic medium of small amounts of phosphatide and of long-chain fatty-acid esters enabled the organisms to grow far more quickly. Thus, with submerged growth technics, testing for tubercle bacilli is becoming both more sensitive and more rapid.

Calcifications, Coccidioidomycosis and Histoplasmosis

The long held dogma that all calcifications within the lung are due to tuberculosis is rapidly being shattered with the discovery of the role played by other micro-organisms. Further evidence of the ability of coccidioidomycosis to produce calcifications is brought out by the studies of Butt and Hoffman,⁵¹ who did coccidioidin tests on 1165 patients at the Santa Fe Coast Lines Hospital in Los Angeles and found that 302, or 26.0 per cent, were positive reactors. The greatest incidence of infection (62.8 per cent) was found in the group of patients coming from the San Joaquin valley. The calcifications of tuberculosis and those of coccidioidomycosis are practically identical, but in some cases the presence of apical scarring (in tuberculosis) helps differentiate the two conditions.

There is some evidence that infection with *Histoplasma capsulatum* may also be responsible for pulmonary calcifications. Palmer,⁶¹ who explored the geographic distribution of histoplasmin sensitivity in the United States by skintesting of 10,580 nurses in eleven different cities, discovered that sensitivity varies widely in different geographic areas, from a low of 5 per cent in and around Minneapolis to a high of 60 per cent in Kansas City, Missouri. In the New England states, 10 per cent of the nurses reacted to the histoplasmin.

To determine the cause of pulmonary calcifications in children in one county in Tennessee, Christie and Peterson⁶² tested 344 with tuberculin, histoplasmin and haplosporangin, and also had chest roentgenograms taken. Calcifications were found in 53.2 per cent, whereas only 21.5 per cent reacted to tuberculin. They regard this as further evidence that in many sections of the United States the prevalence of pulmonary calcifications is far in excess of that which can be explained by tuberculosis as revealed by tuberculin cutaneous testing. It is interesting to note that no child reacted to the haplosporangin, the specificity of the skin reactions thus being demonstrated. Reactions to histoplasmin were observed in 73.2 per cent. Of the group of 78 children who did not react to either tuberculin or histoplasmin, 14 (17.9 per cent) had pulmonary calcifications. Christie and Peterson conclude that present concepts of the primary complex or first-infection tuberculosis in its relation to pulmonary calcification need re-evaluation. The implications of these findings, which challenge a dogma that has existed for many years are nothing short of revolutionary.

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CASE 32331

PRESENTATION OF CASE

A thirty-nine-year-old mechanic entered the hospital because of a chronic cough.

Coughing episodes began twenty years before entry; they occurred about twice a year, lasting two or three weeks and producing about half a cup of greenish sputum daily. Fourteen years before entry the patient had an attack of lobar pneumonia on the left side. Seven years later the cough became chronic, with a slight increase in severity during the winter. The sputum produced was usually greenish but occasionally brownish, yellow or white. It varied in amount daily from half a cupful to two cupfuls when an upper respiratory infection was present. Repeated chest x-ray films taken by a physician were reported as showing only bronchitis.

Two years before entry the patient experienced chest pain for the first time. The pain was localized to the right infraclavicular region and persisted as a steady dull ache, but was not made worse by coughing and never interfered with sleep. Concomitantly he also developed moderate hoarseness. A year before entry the patient began to lose weight and strength and a few months later had hemoptysis. Subsequently he continued to raise a little blood-streaked sputum almost every morning. On one occasion he raised almost a tablespoonful of pure blood. Five months before entry he went to a tuberculosis sanatorium because he felt "run down." A chest film was said to have shown healed lesions at both apexes. Nevertheless he was placed on the waiting list and seven weeks before entry entered the sanatorium for observation. While there he gained 3 pounds and felt much improved, although the morning hemoptyses continued. Three weeks later the right infraclavicular pain had almost disappeared, but a similar dull, steady ache developed in the area of the sixth rib anteriorly, immediately to the right of the nipple line. In addition, there were occasional fleeting dull aches over the left chest anteriorly, localized at various points but chiefly near the apex of the heart. A chest tap attempted

at the sanatorium revealed no fluid. No pneumothorax therapy was given. The patient had never had wheezing, pain on respiration, night sweats or exertional dyspnea. During the year before entry he lost 13 pounds despite a good appetite. On leaving the sanatorium he was told that he did not have tuberculosis.

Five years before entry the patient's brother, with whom he had been living, entered a tuberculosis sanatorium, where he ultimately expired.

Physical examination revealed a well developed and well nourished man in no apparent distress. The right middle and lower lobes of the lung were dull to percussion and showed diminished breath sounds and tactile fremitus. A few coarse, moist rales were heard over the same area. There was no tracheal or mediastinal deviation. The heart was normal.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood revealed a red-cell count of 6,480,000, with 75 per cent hemoglobin, and a white-cell count of 17,650, with 81 per cent neutrophils. Repeated sputum smears were negative for acid-fast organisms.

X-ray studies of the chest revealed a mass at the right hilus within which there were several cavities measuring up to 3 cm. in diameter. In the lateral view the mass was seen to occupy the apex of the lower lobe, with the largest cavity lying posteriorly. There was no involvement of the middle and only partial atelectasis of the lower lobe. Slight scarring was seen at both apexes, and there was some thickening in the region of the right costodiaphragmatic angle.

A bronchoscopy was performed.

DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT To summarize, this patient had a cough of twenty years' duration that began at the age of nineteen. For the first thirteen years this cough was intermittent, occurring in episodes of brief duration and punctuated by an attack of what was said to be lobar pneumonia. During the next five years the cough became continuous and chronic, with a fair amount of sputum, but the x-ray films were said to have shown only bronchiectasis. Two years before entry a new symptom appeared — chest pain, accompanied by hoarseness. In the year before entry constitutional symptoms and hemoptysis appeared, but the x-ray findings were not diagnostic, and it can be assumed that the sputum was negative at the sanatorium. On admission, physical examination showed the patient to be in good condition, without fever, and he had what I assume to be signs of partial bronchial obstruction on the right. Again he had a negative sputum.

We might see the x-ray films at this point.

DR. JAMES R. LINGLEY These are the cavities described lateral to the hilus in the anteroposterior view. In the lateral view they lie posteriorly in the apex of the lower lobe. The cavities are surrounded by considerable density. The whole apex of the lower lobe is involved in this process. This film was taken after tapping the chest, and there is a small amount of air in the pleural cavity, which was not present previously. The diaphragm is possibly a little elevated on the right. The heart shadow is not displaced.

DR. SHORT Is there atelectasis of the right lower lobe?

DR. LINGLEY I think that there is some atelectasis in the apex.

DR. SHORT Is there also a mass in the area of the hilus?

DR. LINGLEY A mass or an area of consolidation.

DR. SHORT Is the mass infiltrating?

DR. LINGLEY Its borders are not at all distinct, but perhaps that is due to atelectasis.

DR. SHORT And you can see no definite mediastinal lymph nodes?

DR. LINGLEY No.

DR. SHORT There are a number of diagnostic possibilities in this case. I might consider what seem to me the unlikely ones first. It does not seem reasonable to explain the whole picture on the basis of bronchiectasis or any usual type of chronic pulmonary infection. One must assume that there was a lesion obstructing the bronchus to the right lower lobe, which was perhaps responsible for the distal pulmonary infection. The absence of mediastinal lymph nodes is against lymphoma with invasion of a bronchus by direct extension. Similarly there is no suggestion of extension into a bronchus from a neoplasm of a neighboring structure, such as the esophagus.

This is not the x-ray picture of sarcoid, and although an infection like actinomycosis can start in a bronchus and cause multiple cavitation, the patient would probably have been sicker, with fever and possibly chills.

Three possibilities therefore remain. The most probable at first glance is carcinoma, that is, a primary bronchiogenic carcinoma. Metastatic lesions that invade the bronchus and simulate primary carcinoma are comparatively rare, and there was no suggestion of a primary lesion elsewhere in the body. The patient had many of the cardinal symptoms of bronchiogenic carcinoma: cough, hemoptysis and dull, nonpleuritic chest pain, although he had no wheezing or dyspnea. There was a mass, if one may call it that, in the region of the right hilus. Cavitation associated with infection distal to such a growth is frequently seen. Hoarseness, not associated with a chest lesion, often indicates cancer, but in this case the lesion seems too low to involve

the nerve supply to the larynx and in any event there is no record of a vocal-cord paralysis. The greatest objection to the diagnosis of primary bronchiogenic carcinoma is the duration of symptoms. The seven-year history of chronic cough seems too long, unless one assumes that the patient had a bronchiectasis of long duration, which was not connected with the lesion that brought him to the hospital. Even the more definite symptoms for two years before admission seem too long not to have produced obvious x-ray and clinical evidence of new growth.

Next tuberculosis must be considered. I meant to ask Dr. Lingley if he saw any evidence of scarring at the apices.

DR. LINGLEY These films, which look very clear to me, do not reveal anything definite at the apices.

DR. SHORT There was a family history of what was probably tuberculosis. The long duration of symptoms suggests pulmonary tuberculosis but not in the face of the negative x-ray films. The repeatedly negative sputum examinations are also against this diagnosis. More than one case of bronchial tuberculosis in this hospital, however, has been diagnosed by bronchoscopy after a negative sputum examination. Still I am forced to reject this possibility and to consider the tuberculosis in this case confusing rather than contributory.

A third possibility is benign tumor of the bronchus. By far the most frequent is the so-called "benign adenoma," which usually occurs in younger people than those with primary carcinoma. Although benign adenoma may be locally invasive and is believed by some to go on to actual malignancy, it grows slowly and is not prone to metastasize. I might mention that in benign adenoma large hemoptyses, with free intervals, are more usual than the repeated slight hemoptyses that this patient had. As an explanation of the cough, I can picture such a tumor's causing long continued irritation and then enlarging to the point of causing bronchial obstruction and distal infection. Perhaps by the time the patient entered the hospital the lesion was actually locally invasive. The relatively good condition of the patient, as well as the symptomatic remission in the sanatorium, is in favor of this diagnosis. I do not believe that a definite diagnosis can be made without the aid of bronchoscopy, but in the light of the whole history benign adenoma presents fewer objections than any other diagnosis.

DR. DONALD S. KING Would you change the diagnosis if you knew that there was one positive sputum examination at the sanatorium?

DR. SHORT That might influence me slightly.

CLINICAL DIAGNOSIS

Carcinoma of lung

DR SHORT'S DIAGNOSIS

Adenoma of bronchus

ANATOMICAL DIAGNOSIS

Epidermoid carcinoma of bronchus (Grade III).

PATHOLOGICAL DISCUSSION

DR KING This was an interesting case. The patient entered Middlesex County Sanatorium with a diagnosis of pulmonary tuberculosis. There was a positive family history in the case of the brother, and the early x-ray films of the patient showed a lesion in the right upper lobe that was not visible in the films displayed here. The lesion at the right hilus, which was seen in these films, was not present when he was first admitted to the sanatorium but was demonstrable after a four-month period, during which moist and musical rales over the right mid-chest in front also developed. The signs and the x-ray findings were observed at the time when Dr Lowrey Davenport was first looking for indications for bronchoscopy in patients with tuberculosis at the sanatorium, and this was the first patient whom he bronchoscoped there. The findings were so striking that he had no difficulty in selling the procedure to the sanatorium doctors in later cases. In this case the tumor mass was so large and friable that a large section was actually coughed into the bronchoscope at the time of its introduction.

Do you want to divulge the diagnosis that was made on that bronchoscopic specimen, Dr Mallory?

DR TRACY B MALLORY The tumor was a highly malignant carcinoma, probably epidermoid in type.

DR KING Because of this finding, a total pneumonectomy was performed. I believe that, so far as the records of the Massachusetts General Hospital are concerned, this is one of two patients who are now living five years after a removal of a lobe or entire lung for bronchiogenic carcinoma. The patient has been under observation in the hospital recently because of an acute infection in the remaining lung. He recovered satisfactorily.

DR MALLORY He now has survived nine years.

DR SHORT Were there positive lymph nodes in the hilus?

DR MALLORY No. The tumor was at the junction of the middle-lobe and the lower-lobe bronchus. It was an ulcerated lesion, nearly 2 cm in diameter, and the histologic appearance was that of a highly malignant tumor. This is the last case on which I should have given a favorable prognosis, and strangely enough the patient presents our best result.

DR KING Perhaps the fact that the diagnosis was made the sigearly is nificant point in this case. The symptoms, signs and x-ray findings were discovered

at an early date, because he was in the sanatorium during this period.

DR SHORT You assume that the previous symptoms were due to tuberculosis?

DR KING I do not know just how many of the symptoms were due to tuberculosis, but I had understood that the surgical specimen showed not only cancer in the right lung but also a tuberculous cavity. We have therefore always spoken of this case as a combination of both tuberculosis and carcinoma. I may be wrong in my memory of the pathologist's report on the surgical specimen.

DR MALLORY We have no record of tuberculosis.

CASE 32332

PRESENTATION OF CASE

First admission. A forty-three-year-old Chinese laundryman entered the hospital because of persistent cough with hemoptysis.

The history was not easy to obtain, because of language difficulties. The patient was apparently well until a year and a half before admission, when for the first time he coughed up about a cupful of blood. Subsequently he continued to have hemoptyses at irregular intervals varying from one to several weeks. The cough was worse in the morning, during the winter months and in the presence of upper respiratory infection. Occasionally it was accompanied by a sharp pain in the left epigastrium. The appetite became poor, and during a period of four months the patient lost about 8 pounds. There was no weakness or fatigue. Fifteen months before admission, the patient was seen in the Out Patient Department. An x-ray film of the chest at that time revealed increased density in the region of the lingula and both lower lobes. The left lower lobe appeared to be nearly completely collapsed in the basilar segment, but the dorsal division did not seem to be involved. Within the collapsed lobe there were dilated bronchi. There was also beginning dilatation of the lateral division of the lingular bronchus of the left upper lobe and of the anteromedial bronchi of the middle lobe, as well as the anterior division of the right lower-lobe bronchus. Bronchoscopy showed moderate hemorrhagic bronchitis of the left lower lobe, with questionable bronchiectasis. Repeated sputum smears were negative for acid-fast organisms. Twelve months before entry, the patient entered a state hospital because of the continued cough and hemoptyses. He remained there until his admission to this hospital. Serial sputum examinations had shown no tubercle bacilli.

The patient gave no history of tuberculosis or exposure to it. He had had an attack of "pneumonia" as a young man.

Physical examination revealed a well developed and well nourished man in no acute distress and coughing only infrequently. The sputum, however, was foul and contained frothy blood-tinged material. Percussion of the chest revealed some dullness at both bases posteriorly and slight dullness below the right axilla. There were coarse rhonchi in the right upper chest posteriorly and also a few on the left. Breath sounds seemed slightly diminished over the right chest anteriorly and laterally. The heart and abdomen were normal. The tendon reflexes of the left arm were somewhat hyperactive, and there was some weakness and flabbiness of the left hand. The fingers of both hands showed early clubbing.

The temperature, pulse and respirations were normal. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,600,000, with 11.3 gm of hemoglobin, and a white-cell count of 6600, with 71 per cent neutrophils and 19 per cent lymphocytes. The total protein was 8.2 gm per 100 cc. The urine was normal.

X-ray examination of the chest, including bronchograms, showed no change from the previous findings, the most marked bronchiectatic process being in the left lower lobe.

The patient was discharged on a high-protein diet.

Second admission (three weeks later). The patient was readmitted for surgery. Since discharge he had continued to cough up daily about 100 cc of foul, gray sputum, but there had been no further hemoptyses. Physical and laboratory findings were essentially the same as on the previous admission. The patient was placed on aerosol penicillin to reduce the amount of sputum. On the fourteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR REED HARWOOD. The diagnosis in this case involves a discussion of the causes of bronchiectasis. Bronchiectasis may be defined as a chronic progressive disease of the bronchi, with bacterial invasion of the bronchial wall and the surrounding lung tissue. It results in an inflammatory reaction of the bronchial wall, dilatation of the bronchus and varying degrees of inflammatory reaction and fibrosis of the adjacent lung. Different sorts of mechanical forces are said to account for the bronchial dilatations. For example, in the presence of obstruction of a bronchus, coughing increases not only the intrabronchial pressure distal to the obstruction but also the difference between the intrapleural and the intrabronchial pressure with each inspiration. It is believed that most cases of bronchiectasis are caused by obstruction of the involved bronchus as well as by infection. The infecting organisms may be any of the pyogenic bacteria, as well as spirochetes and fusiform bacilli, the tubercle bacillus and other less frequent organisms. The

usual sequence of events in the development of bronchiectasis is repeated attacks of bronchitis, often associated with chronic sinusitis. Unresolved pneumonia or repeated attacks of bronchopneumonia may also initiate the process. In the case under discussion it seems probable that the bronchiectasis had its beginning when the patient had pneumonia as a young man. The history of chronic cough, which was worse in the morning, during the winter and during respiratory infections, is typical, as is the character of the sputum, the periodic hemoptyses and the clubbing of the fingers. Indeed, there is little in the record to suggest that this case does not fall into this category. I believe that the patient was prepared for left lower lobectomy with this diagnosis in mind.

Some of the other conditions that cause bronchiectasis must be considered. Tuberculosis was obviously suspected in this case. Repeated failure to find tubercle bacilli in the sputum is strong evidence against this diagnosis. It is extremely probable that while the patient was at the State Hospital the stomach contents were examined for tubercle bacilli. Tuberculosis most frequently involves the apexes of the lungs, but its absence in these areas does not exclude it from consideration. A tuberculous ulceration of the lower main-stem bronchus, however, would probably have produced a rapid spread of the disease and a downhill course. A tuberculous stenosis in this region would have been visible to the bronchoscopist. The involvement of bronchi going to several lobes is against a localized tuberculous lesion.

Could a tumor have caused the bronchiectasis? Benign and malignant intrabronchial tumors cause obstruction to the bronchus with infection beyond the obstructed area, as do tumors of mediastinal lymph nodes and infected lymph nodes. One would expect, however, to find the bronchiectasis confined to the involved segment. Besides, the bronchoscopist would be able to see the obstructed area. The same reasoning applies to the presence of a foreign body in the bronchus.

Much rarer causes of bronchiectasis are actinomycosis and other mycotic infections. I assume that the presence of sulfur granules or yeast cells would have been detected in some of the many sputum examinations. In actinomycosis the constitutional symptoms are apt to be severe, and there is a tendency to sinus formation and particularly to abscesses that drain through the chest wall.

Mention is made of increased reflexes in the left arm, with weakness and flabbiness of the left hand. Without more precise neurologic findings, it is difficult to connect this observation with the pulmonary disease, especially since the lesions in the lung were too low to have produced symptoms of brachial plexus. Metastases of tumor could, of course, account for such a finding, but I do not consider the data sufficient to make a definite diagnosis.

In summary, I believe that this patient had bronchiectasis as a result of repeated upper respiratory and bronchopulmonary infections. Tuberculosis is my second choice, but there is little evidence to support this diagnosis. The diagnosis of tumor or other unusual causes of bronchiectasis remains in the realm of speculation.

CLINICAL DIAGNOSES

Bronchiectasis

DR HARWOOD'S DIAGNOSIS

Bronchiectasis of left lower lobe

ANATOMICAL DIAGNOSES

Bronchiectasis of left lower lobe.

Pulmonary tuberculosis

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY: This patient was operated on with a preoperative diagnosis of bronchiectasis, as Dr Harwood suggested, and a lobectomy was done. The presence of extensive bronchiectasis was confirmed, but no obstruction of the major bronchi was found. There was a marked chronic inflammatory process in the lung parenchyma as is often present in cases of bronchiectasis, and the one surprise was that scattered through this inflammatory tissue were nodules of tuberculous infection. Most of these were fairly well healed, but one or two still had frankly caseous centers, a few giant cells and some probable degree of activity, although I am inclined to believe that the tuberculosis was coincidental and not responsible for the primary lesion, which was certainly bronchiectasis.

DR DONALD S KING: You have not often found tuberculosis in lobes that have been removed?

DR MALLORY: Very seldom indeed.

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STATUS OF NATIONAL HEALTH LEGISLATION

THE stormy seventy-ninth session of Congress has terminated without the enactment of proposed health legislation, which has been surrounded with controversy and recrimination since the first committee hearings. Proponents of the Wagner-Murray-Dingell Bill have postponed their efforts to obtain enactment until Congress reconvenes in January, 1947, and the Pepper Bill has not been reported out of committee.

A respite is thus granted in which the medical profession can marshal its forces for the fight when these bills come up for consideration during the eightieth session of Congress. Organized medicine also has an

opportunity to initiate action that will make the threatened legislation unnecessary.

Senate Joint Resolution No 177, introduced by Senators Pepper and Taft on instructions from the Senate Committee on Education and Labor, fills a need that has been greatly felt and also demonstrates what may be a healthy trend away from the type of governmental control and participation embodied in the Wagner-Murray-Dingell and Pepper bills. The resolution amends the Social Security Act to provide for increased grants to the states for crippled children, maternal and child health and child welfare, favorable action on the resolution — which has still to be considered by the Senate Finance Committee and the House Appropriations Committee — would establish over the funds concerned regulations and controls similar to those already in effect on appropriations for the Children's Bureau. Legislation that takes the form of badly needed aid for existing welfare agencies — rather than that of creating a spate of new bureaus and extending regimentations and control to fields that should be beyond the concern of the Government — is always welcome.

Another encouraging note is provided by Senate action on President Truman's reorganization plan, which transfers the Children's Bureau from the Department of Labor to the Federal Security Agency and thus affords an opportunity for co-ordination between the Bureau and the United States Public Health Service and similar agencies.

NEW ANTIMALARIAL DRUGS

DURING the past eight months, the discovery of two new antimalarial drugs has been announced. One, called "paludrine" (M 4888), was produced in England,^{1 2} and the other SN 7618, which was later called "chloroquine," was developed in this country and announced by the Board for the Co-ordination of Malarial Studies.^{3 4} Both drugs are the result of extensive efforts on the part of British and American scientists during World War II to find new chemotherapeutic agents for the prophylaxis, suppression and treatment of malaria.

The initial and urgent need for an extensive research program on the chemotherapy of malaria arose out of the grave problem of malaria control and treatment among the armed forces in World War II. The loss of the main source of cinchona bark for the production of quinine and the questionable value of quinacrine (Atabrine) furnished the driving force for research into the fundamental facts about malarial parasites, the disease that they produce and the chemotherapy of the disease. The achievements and value of the program are now becoming apparent.

Aside from the fundamental information that helped define the problems involved in suppressing and curing malaria, over fourteen thousand compounds were tested for their activity against avian malaria in this country and eighty of these compounds were subsequently tested on cases of human malaria. In addition, over one thousand compounds were made and tested in England.⁵

Coincident with this vast search for new effective drugs, experimentation with quinacrine proved that different dosage schedules, employing larger doses, were needed to produce and maintain effective plasma levels for suppression and treatment.⁶ This information helped to explain previous difficulties with the drug. The new dosage schedules caused a dramatic reversal in the trend of malarial incidence among the armed forces. Malaria could be suppressed, and a radical cure of falciparum malaria could be effected, but quinacrine continued to fail as a true casual prophylactic and as a radical cure for relapsing vivax malaria, particularly with strains of Pacific origin. Although the new quinacrine therapy was of strategic value in winning the war, the search for more effective drugs continued.

The reasons for the failure of quinacrine and quinine to produce radical cures of vivax malaria

and to prevent the relapsing nature of the disease in a majority of cases are slowly becoming understood. These drugs are effective against all stages of the parasites in the blood stream, but they are apparently unable to penetrate other cells and thus to sterilize the more or less hypothetical tissue stage of the plasmodia. These tissue stages, which develop from the sporozoites injected by the infective

mosquitoes prior to invasion of the blood stream and the erythrocytes, have been seen and studied in several types of avian malaria.⁷ The experiments of Fairley⁸ and his collaborators suggest that they also exist in human malaria. Thus an effective drug must presumably penetrate selectively and exert a lethal effect on the parasites within the cells of such organs. This process appears to be

necessary for true casual prophylaxis, radical cure and the prevention of relapses.

With the above information, the English scientists decided to explore some new ring system that would satisfy the requirements for antimalarial activity against the tissue stages of the parasites.⁹ Compounds known as pyrimidines were chosen for the initial studies because of their physiologic importance in the synthesis and function of cell nuclei. That this choice was a fortunate one was soon verified by the discovery of antimalarial activity in a derivative of anilino-pyrimidines called "2666."

The evolution of paludrine from 2666 is an exciting account⁹ and a prime example of the type of achievement made possible by a closely co-ordinated collaboration between scientists from different fields. It is sufficient to say here that paludrine is N_1 -p-chlorophenyl- N_4 -isopropyl biguanide and that the compound is "a chemical type not hitherto met with in chemotherapy."⁸ The antimalarial activity of this drug initially demonstrated in cases of human malaria in England has been substantiated by field

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trials at Cairns, Australia^{10, 11} The drug has been shown to be a true casual prophylactic and to produce a radical cure of malignant tertian malaria. With vivax malaria, paludrine is a partial casual prophylactic, tests regarding radical cure were not completed, but a dosage of 0.1 gm twice a week appeared to prevent relapses indefinitely. Furthermore, the difference between the therapeutic and the toxic dose was found to be great enough to permit a wide latitude in therapy without danger to the patient.

Although detailed accounts about the discovery and therapeutic trials of chloroquine have not appeared, the story of this new antimalarial drug is probably just as fascinating. Here again, falciparum malaria is cured radically but vivax malaria is more resistant to treatment. The primary attributes appear to be the small dosages that are effective in producing radical and clinical cures, it has approximately three times the antimalarial activity of quinacrine and causes no discoloration of the skin.⁴ Since this drug has been tried on over 5000 cases of human malaria, judgment concerning its efficacy rests on firmer ground than does that for paludrine. Reports of well controlled field experiments comparing the simultaneous effects of the two drugs will, however, be awaited with great interest.

Those who know the malarial problems awaiting control and eventual solution are well aware that the existence of two new drugs cannot achieve the desired results. The combined efforts of governments, peoples and specialists in malariology utilizing drugs, antianopheline campaigns and new insecticides are needed for effective malaria control.

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MASSACHUSETTS MEDICAL SOCIETY

DEATH

MESERVE — Faith L. Meserve, M.D., of Weston, died July 19. She was in her fifty-second year.

Dr. Meserve received her degree from Boston University School of Medicine in 1926. She was a fellow of the American Medical Association.

Her mother, two sisters and a brother survive.

MISCELLANY

DR. JOHN E. FISH — AN APPRECIATION

Massachusetts has long taken pride in its pioneering leadership toward social improvement and cultural achievement. Here in Massachusetts John Harvard founded the first college. In later generations, Horace Mann fathered public-school education as it is known today, Dr. Samuel Howe organized the Perkins Institute for the Blind, and Laura Bridgman and Helen Keller, without sight or hearing, gained liberal educations. In line with these traditions, the excellent St. Botolph Street School for Crippled Children was founded for the purpose of extending education to children whose physical disabilities prevented their attending the regular schools. It soon became apparent, however, that a day school could not meet the full requirements for educating all the cripples in the Commonwealth. In 1904, the Massachusetts Legislature therefore created a novel institution to serve as a public boarding school, with hospital facilities available to all disabled children, whether rich or poor.

The opening of the Hospital School was delayed for four years while land was purchased and the first buildings erected. During this interval, one of the greatest difficulties had been to find a man qualified to serve as superintendent. In 1908, by rare good fortune, the trustees selected Dr. John E. Fish for this difficult post, and nowhere could they have found a man better qualified for these new and untried duties. Born in Vermont, the son of a country doctor, he was already steeped in the fine traditions of the medical profession, to which he added his own liberal education at Dartmouth College and Medical School. He had gained administrative experience in some of the state institutions and had acquired a clear insight into human character through the patients he dealt with there. More fortunate still, Dr. Fish was blessed with a wife ideally suited to help in the life of such a school as this. She was the daughter of a Civil War surgeon who spent his later years in family practice in Vermont. With her refinement, quiet humor and unfailing cheerfulness, she brought to her husband the help that a man needs most under difficulties. Thus Dr. Fish was the perfect choice in every respect, to face the unforeseen problems and difficulties of the new institution. Time has tried him for thirty-eight years, during which he has carried the school through good times and bad, through the upheaval of two world wars and into the second postwar era. Without a break in his long service, he has been reappointed by governors of both major political parties. He has outlived the members of the original Board of Trustees who founded the school and has served under the chairmanship of the son of one of them, the sons of three of the doctors on the earlier consulting staffs have taken the places of their fathers beside him. From the beginning and without faltering, he has fulfilled and advanced the highest hopes of those who first conceived of the institution. As one of the present trustees has remarked: "The school was merely a dream when it was planned. Fish has made that dream come true."

The extent of his achievement in giving reality to such a dream can be measured only by the lives it has liberated from crippled helplessness into the freedom of self-supporting and educated citizenship. It is difficult to appreciate the neglect of educational opportunities for handicapped children during the early years of this century. In the beginning, the school's admissions included many children who had grown into adolescence without a single day's schooling. At the age of fourteen and fifteen, these boys and girls were given their first lessons in elementary reading and writing. Every form of disability was represented among the applicants, but no

matter how completely helpless the child appeared physically, none were denied the opportunities of learning provided they had the capacity to understand. One girl, who was born without hands went to the school at the age of four. After graduation from the eighth grade, she took a stenographic course and learned to write shorthand at a rate of one hundred and twenty words a minute. She has gone on to the study of art and has painted some creditable portraits. This girl is only one of the many whose physical handicaps would have seemed totally disabling in any other locality but whose development at the school has been possible. They came as children with useless limbs and twisted backs, or confined to crutches and wheel chairs or with halting, unbalanced gaits or perhaps unable to get off a litter. But they acquired the spirit of strength and independence, the will to do for themselves, and they left equipped with knowledge equivalent to that of any normal children in similar grades. In all, there have been six hundred and forty-one graduates of the school, a large number of whom have become self-supporting and many of whom are raising and supporting their own families. Most of them have found specialized jobs of one type or another. Some, however, have carried their education on into further fields. Thus, two have won seats in the Legislature, two are artists, two are lawyers, one a doctor, another a nurse and still another a social worker. Seven of them have returned to serve on the staff of the school—one as treasurer, and one as head of the school department. Seven outgrew their physical handicaps and served in the armed forces during the war.

Three general ideas that have formed the basis of Dr Fish's program can best be described by quotation of his own terse phrases. The first of these is the declaration; "Education of a crippled child is not a charity any more than the education of a normal child." One might say that such a statement seems self-evident, yet it was not always so regarded, nor has any state in the Union other than Massachusetts gone to such lengths in giving this thought practical fulfillment. In the early years of the school, a well meaning critic once objected that money spent on the education of a crippled child would be wasted unless the child could be made self-supporting. To this objection, one of the school's founders replied "That is not the way our Saviour looked at it. He said, 'Give life, and give it more abundantly.'" Throughout his career, Dr Fish has clung to that doctrine, and it is suitably inscribed on the memorial clock tower that the graduates have dedicated to him.

As a second principle, Dr Fish believes, "No form of surgical care or other treatment can be regarded as complete that neglects the social, moral and mental growth of the child." This statement clearly exposes the most serious defect in other programs for crippled children: too many private, state and federal institutions offer only operative or postoperative surgical treatment, not recognizing that partial correction of a physical deformity still leaves a crippled mind and not realizing that in the months, and often the years, spent in clinics and hospital wards and convalescent centers, the child loses invaluable time both from textbook lessons and from character-building experience. Such lessons and such experience must come early enough to help the child develop the right mental attitude, if they are postponed too long, the damage to the child's mental processes may be irreparable. As the trustees observed in their first report "Disabled children who have been too tenderly cared for much beyond the age of puberty are liable to develop a lack of initiative and indolence that is difficult to overcome. A pauperization of character has been developed." The ideal of the Hospital School has therefore been to allow education, surgical care and convalescence to proceed together—and note that education is given first place.

Perhaps the most important basis of the school's success is explained in Dr Fish's third and vital maxim, "It has been found that the placing of crippled children under healthful conditions, thus directly stimulating opportunities for play, study and amusement, tends to destroy any source of self-pity and teaches them to minimize or forget their disabilities." By this concept, the role of education is extended beyond ordinary schoolbook instruction and reaches a personal, psychologic, almost spiritual perspective. It aims at improving character, so that these children may grow to a richer, more self-sufficient maturity. That, essentially, is what the Hospital School has succeeded in doing with the invalids who are enrolled as students. For the fulfillment of

this purpose, it was recognized that even crippled children are dominated by normal cravings for games and social activities, and that such activities constitute a necessary part of their development. There is not space to describe the numberless methods, large and small, that Dr Fish employed to carry his thought into action. One example will serve to illustrate the rest. This was the organization of a baseball team on which each boy was allowed to play so far as his own abilities permitted. The legless pitcher, who trained himself to strike out normal boys of the local schools, will always be remembered, as will the batter with artificial legs who was supplemented by an armless boy running bases. No matter how the score stood with their rivals, such teams defeated their own disabilities, which were their real opponents. The same principle was carried to all the school's activities. Musical talents were cultivated by choir singing and by the organization of a school band. A shop for watch repairing under the tutelage of an expert craftsman has been eagerly attended. The dormitories were made as home-like as possible, and the girls were encouraged to help in cooking and serving meals. The girls of the senior class were given a beautifully furnished reception room, where they served afternoon tea once a week to guests and callers. The local clergy have co-operated, and Catholic, Protestant and Jewish services are held at the school every week. Thus, so far as possible, the children learn to lead normal lives in an optimistic, healthful and happy environment.

Based on these principles, the Hospital School has become a permanent institution in the life of the Commonwealth. It is still unequalled and unrivaled anywhere else in the world. Its traditions are now so well established that one can look forward to another generation of service on a level with what it has already produced. Now, as he retires from his duties, one feels more keenly than ever gratitude and appreciation for Dr Fish's high-minded vision and for the devoted service and strong and wise leadership that made a dream come true.

C H B

NOTICES

ANNOUNCEMENTS

Dr H Myer Bloomenthal announces his return from military service and resumption of practice of medicine and surgery at 1396 Commonwealth Avenue, Boston

Dr Leon Ryack, having returned from military service announces the opening of his office for the practice of medicine at 1755 Beacon Street, Brookline

Dr Maurice M Tolman has returned from naval duty and will resume the practice of dermatology at 636 Beacon Street, Boston

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination (Part I) of the American Board of Obstetrics and Gynecology for all candidates will be held in various cities of the United States and Canada on Friday, February 7, 1947, at 2:00 p.m. Candidates who successfully complete this examination proceed automatically to the Part II examination held later in the year. All applications must be in the office of the Secretary by November 1, 1946. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

A number of changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept a nine-month residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration (April 1, 1946).

Applications are now being received for the 1947 examinations. Final examinations will be held in Pittsburgh June 1 to 7, 1947. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

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ACUTE GENERALIZED MILIARY TUBERCULOSIS IN ADULTS*

A Clinicopathological Study Based on Sixty-Three Cases Diagnosed at Autopsy

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BOSTON

ACUTE generalized miliary tuberculosis is a condition that results from the sudden and often overwhelming hematogenous dissemination of tubercle bacilli from an established focus to many of the organs of the body. The large number of small, acute tubercles that develop in these organs have been said to resemble millet seeds in size and appearance, whence stems the adjective "miliary." The clinical course is so varied that diagnosis before death is often not achieved. The condition should be rigidly differentiated from the various forms of nonprogressive or slowly progressive, more or less localized forms of disseminated tuberculosis. The hematogenous dissemination of occasional tubercle bacilli from chronic foci in the lungs or elsewhere frequently results in the various forms of chronic disseminated tuberculosis so often seen at autopsy. Pennington¹ found that 68 per cent of 200 cases of pulmonary tuberculosis at autopsy showed extrapulmonary foci of a chronic type, lesions that Krause² terms "benign generalizations" of pulmonary forms of tuberculosis. Hegler³ points out that when occasional tubercle bacilli are released, producing isolated tubercles in one or two additional sites, the disease has in a sense become generalized but is still quite distinct from acute generalized miliary tuberculosis. Kayne, Pagel and O'Shaughnessy⁴ believe that acute, fatal disseminations occur in an extremely small percentage of affected persons but that some 40 per cent show evidence of hematogenous dissemination at autopsy. Most of the cases fall in the group that these authors term "abortive hematogenous dissemination," and the extrapulmonary lesions are generally nonprogressive.

One must recognize, therefore, that disseminated tuberculous infection may appear in several forms. One extreme is the acute, progressive disease, which is the subject of this survey, the other extreme is the

chronic, nonprogressive extrapulmonary tuberculous lesion, which seldom, if ever, causes death.

All the autopsy reports for the Boston City Hospital over a five-year period (1937-1941, inclusive) were reviewed. In selecting cases for the series, two important exceptions were made, as follows: none of the autopsy material from the Sanatorium Division was utilized, and cases in patients less than twelve years of age were excluded owing to the fact that the autopsy material included a disproportionately small number of children. We have thus concerned ourselves exclusively with the condition as it occurred in adults in this, a general, hospital.

INCIDENCE

General

Acute generalized miliary tuberculosis is generally considered to be a rare condition. Lewison et al.⁵ reported that 1.09 per cent of 8800 consecutive autopsies at Cook County Hospital showed the condition. Our own data indicate that 1.55 per cent of the 4066 cases autopsied at the Boston City Hospital between 1937 and 1941 showed acute generalized miliary tuberculosis. Of considerably greater interest is the frequency with which the condition is present in cases showing some more chronic type of tuberculosis. Fishberg⁶ states that of patients suffering from pulmonary tuberculosis in any of its forms, about 1 in 20 dies with symptoms of miliary dissemination of tubercle bacilli, and approximately the same figure is given by Simmonds.⁷ In Lewison's series the condition was found in 11.9 per cent of tuberculous cases. Auerbach⁸ reviewed 1656 consecutive autopsies on patients with tuberculosis, in 17.9 per cent of which acute generalized miliary tuberculosis was demonstrated. We reviewed autopsies on 4066 patients, in 310 of which (7.6 per cent) tuberculosis of some sort was present. In this group of 310 cases, there were 63 cases of acute generalized miliary tuberculosis (20 per cent). Our figures are somewhat analogous to Lewison's in that they represent the incidence of the condition at

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autopsy in a general hospital, but they are not truly analogous in that owing to the nature of the autopsy material children have been excluded from the series

By Sex

Litten,⁹ in one of the classic articles on the subject, stated that acute generalized miliary tuberculosis is more frequent in men than in women, and Fishberg⁶ is in agreement. Hartwich,¹⁰ however, reviewing 200 cases of the disease, found that 51 per cent of the patients were females and 49 per cent were males. In our series of 63 cases, there were 44 men (70 per cent) and 19 women (30 per cent). Of the 310 patients in whom some type of tuberculosis was found at autopsy, however, 69 per cent were males and 31 per cent were females. Hence the sex incidence of acute generalized miliary tuberculosis in this series is not significantly different from that for tuberculosis of all types. Furthermore, in this hospital more autopsies are permitted on men than on women, and we are of the opinion that the alleged sex difference in the incidence of the condition is more apparent than real.

By Age

That the disease may occur at any age is generally agreed. Its occurrence in the earliest weeks of life has been noted by Hegler,³ who reviewed the cases of this type reported up to 1923. Transmission of the infection to the unborn child by the maternal and placental circulations has been suggested, and we noted 1 case in which such a process may have occurred.

The highest incidence of the disease is said by some authors^{3, 8, 11} to occur in the second and third decades. In Hartwich's¹⁰ series the peak incidence

incidence of nonmiliary forms of tuberculosis at the Boston City Hospital, which, surprisingly enough, was in the seventh decade. Our findings are not necessarily at variance with the statements by Hartwich and by Amberson, since no children were included in this series. Among adults, however, the disease was more frequent in the younger than in the more advanced age groups.

It is of interest to note that although peak incidences occurred as indicated, acute generalized miliary tuberculosis is by no means unknown in the seventh, eighth and ninth decades. Thirteen per cent of Hartwich's and 14 per cent of Braun's¹² patients were over sixty years of age. Thirty per cent of our patients were over that age, and 16 per cent were over seventy years of age. The oldest patient was eighty-five and the youngest nineteen.

CLINICAL ASPECTS

Diagnosis

In this series the ante-mortem and post-mortem diagnoses of tuberculosis were as given in Table 2.

TABLE 2 Clinical Diagnosis and Findings at Autopsy

DIAGNOSIS	DIAGNOSED CLINICALLY	FOUND AT AUTOPSY
Fibrocasseous pulmonary tuberculosis	36	45
Acute generalized miliary tuberculosis	16	63
Tuberculous meningitis	7	7
Tuberculosis of larynx and pharynx	6	2
Tuberculous cervical adenitis	5	—
Tuberculous peritonitis	4	4
Tuberculosis of gastrointestinal tract	4	27
Tuberculosis of bone	2	4
Tuberculosis pericarditis	2	4
Tuberculosis of epididymis	1	4
Tuberculosis of kidney	1	6
Tuberculosis of testicle	1	1
Tuberculous pancreatitis	1	1

In this hospital, the larynx, pharynx and cervical lymph nodes are not routinely examined at autopsy, so that figures for these sites are probably artificially low. The large discrepancy between the clinical and the pathological diagnosis of gastrointestinal tuberculosis is probably due to the obscurity and relative unimportance of the associated symptoms.

As shown, the ante-mortem diagnosis of miliary tuberculosis was made in 16 of the 63 cases (25 per cent), and 2 additional cases were tentatively so diagnosed. A survey of these 16 cases disclosed that the majority were diagnosed on the basis of x-ray examination of the chest. Several cases, however, were apparently diagnosed largely on the basis of the clinical course, the presence of known chronic tuberculosis and the leukocyte picture. Our diagnostic average compares rather unfavorably with that reported by Lewison,⁵ who apparently found that 75 (78 per cent) of the 96 cases of acute generalized miliary tuberculosis demonstrated at autopsy at Cook County Hospital were diagnosed clinically.

TABLE 1 Age Incidence of Acute Generalized Miliary Tuberculosis and of Nonmiliary Tuberculosis Among Adults at Autopsy*

AGE	TOTAL CASES WITH NONMILIARY TUBERCULOSIS		TOTAL CASES WITH MILIARY TUBERCULOSIS	
	NO.	PERCENTAGE	NO.	PERCENTAGE
15-19	2	—	2	3.2
20-29	10	4.5	13	20.6
30-39	24	9.7	7	11.1
40-49	39	15.8	11	17.5
50-59	46	18.6	11	17.5
60-69	55	22.0	9	14.3
70-79	46	18.6	9	14.3
80-89	10	4.5	1	1.5
90 and over	1	—	0	—
Unknown	14	5.5	0	—
Totals	247		63	

*Chi square = 23.0, when N = 5. P = less than 0.01.

occurred in the first decade. Amberson¹³ states that acute generalized miliary tuberculosis occurs most frequently in babies and young children. In the present series, the peak incidence (Table 1) was found in the third decade. In contrast is the peak

History and Symptoms

A history of exposure to active tuberculosis was obtained in 16 per cent and a history of previously active tuberculosis in 26 per cent of the 35 cases in which specific inquiry was made.

Anorexia, weight loss and cough were the most prominent symptoms, occurring in 90, 85 and 82 per cent, respectively. Night sweats, dyspnea, chest pain and hemoptysis were recorded in 79, 64, 49 and 15 per cent, respectively. Any or all of these symptoms may occur in fibrocaceous pulmonary tuberculosis without miliary dissemination and did not, for this reason, serve to establish the correct diagnosis in any of our cases. In several cases, however, the rapidity of onset and the severity of symptoms appear to have been of assistance in arriving at the correct diagnosis. Dyspnea was not significantly more frequent in the group of cases that showed massive involvement of the lungs by the miliary process than it was in the group that did not. Hemoptysis was seen in 6 cases of the entire series, and in 5 of these chronic pulmonary lesions as well as miliary involvement of the lungs were present at autopsy. Cough was equally prominent in both groups. Pronounced dyspnea was usually seen as a terminal finding but apparently provided little or no specific diagnostic assistance.

Seven patients presenting neurologic signs and symptoms were diagnosed clinically as having tuberculous meningitis, and the diagnosis was confirmed at autopsy in all. This incidence (11 per cent) is lower than that reported by most authors, probably because children were excluded. It is generally agreed that the more children included in any series, the higher the incidence of tuberculous meningitis.^{3, 11, 14}

Physical Findings

Physical findings in acute generalized miliary tuberculosis are seldom of much diagnostic assistance. In many of these cases, physical examinations were necessarily cursory and incomplete, and in only 1 case was a physical finding diagnostic (see below).

The course of the temperature in the disease was described by Cornet¹¹ as having no definite form and showing irregularity as its most characteristic feature. Hegler³ found true hectic fever of the so-called "picket-fence" type and continued typhoid fever in some of his cases, but stated that the irregular remittent type was the most frequent. The latter type is characterized by irregular and unpredictable rises of temperature to 102 or 103° F every few days, the temperature falling to lower but not to normal values between rises. Afebrile cases are described by most writers, and are said in the older literature to occur most frequently when such complications as tuberculous meningitis, cardiac insufficiency or extreme age are present. After a careful survey of the temperature charts in this series we find ourselves

in complete agreement with Cornet. We could find no feature that was common to the entire group, and many of the charts were so irregular as to defy classification, although about one third of them fit roughly into the irregular remittent category. True "picket-fence" charts were noted in 4 cases, and *typus inversus* charts in 3. The highest temperatures in the entire series were found in one of the cases of *typus inversus* temperature, the maximum reading being 107° F. All 7 of the cases in which tuberculous meningitis was found showed elevated temperatures, and no such depression of temperature as has been frequently described in the past was found in the group.

Rapid pulse rates were the rule, and tachycardia out of all proportion to the temperature was seen in many cases. Sixty per cent of the patients had sustained pulse rates of 120 or higher, and terminal elevations to 160 in association with terminal tachypnea were frequent.

A pronounced increase in the respiratory rate has been thought to indicate diffuse miliary involvement of the lungs.³ An attempt to correlate rapid respiratory rates with miliary involvement of the lungs in this series met with complete failure, and we doubt that the segregation of a clinical group as pulmonary miliary tuberculosis on the basis of marked increase of respiratory rate is justified. Sustained elevations of the respiratory rate to 30 or higher were present in 60 per cent of the series, and terminal tachypnea associated with cyanosis was present in almost all the patients.

The general appearance of most of the patients was consistent with that seen in any acute febrile illness. The state of nutrition on entry to the hospital was given as poor in 62 per cent, good in 25 per cent and excellent in 8 per cent. It is interesting to note that several patients were frankly obese but lost weight rapidly during the relatively short course of the disease.

Clubbing of the fingernails was noted on physical examination in 4 cases, 2 of which showed fibrocaceous pulmonary tuberculosis, on which pulmonary miliary involvement was superimposed. In the other 2 cases the lungs at autopsy showed miliary lesions but no chronic tuberculous involvement, suggesting that clubbing is not necessarily dependent on chronic pulmonary changes but may be produced by acute miliary involvement of the lung alone.

Ophthalmoscopic examination disclosed the presence of miliary tubercles of the ocular fundi in 1 case. This observation represents the only physical finding in the series that was diagnostic of acute generalized miliary tuberculosis. Several authors, including Litten,⁹ state that miliary involvement of the ocular choroid is a frequent occurrence. Choroidal tubercles are said to be bilateral and to appear as pale, grayish-white oblong patches with indistinct edges. In the early stages, the di-

iameter of such tubercles seldom exceeds 1 mm. When caseation takes place, a central depression may develop in the lesion.³ Although such tubercles may be confused with other ophthalmoscopic findings, their presence is said to be pathognomonic of acute generalized miliary tuberculosis. We are not able to comment further on this important phenomenon, since few adequate ophthalmoscopic examinations were carried out.

Pulmonary findings consistent with the diagnosis of chronic pulmonary tuberculosis, usually apical in location, were reported in 36 cases. In 29 of them the disease was found at autopsy as diagnosed clinically. Of the 63 cases in the series, 18 were found at autopsy to show miliary involvement of the lungs in the absence of chronic pulmonary tuberculosis. No chest signs of any type were found on physical examination in 4 cases, diffuse fine to medium rales were found in 6, and various other nondiagnostic signs were encountered in the remaining 8 cases.

Enlargement of the *spleen* has been frequently reported in the literature as occurring in acute generalized miliary tuberculosis. Litten⁹ found a palpable spleen in 70 per cent of his cases. Hegler³ states that splenomegaly in the disease is frequent but that gross enlargement of the spleen is extremely rare. Amberson¹² holds that the spleen is palpable in a minority of cases. It is generally recognized that enlargement of the spleen at autopsy does not necessarily mean that the organ was palpable during life. In addition to the weight of the spleen, its palpability depends on other factors, including the experience of the examiner, the thickness of the abdominal wall and the degree to which the patient is able to co-operate. Obviously a spleen that is greatly enlarged by weight may not be palpable clinically if other factors are not favorable. We believe that a spleen weighing over 400 gm. should be palpable clinically, particularly if careful and repeated examinations are carried out. Under optimal conditions, spleens weighing considerably less may also be palpable. Abdominal palpation was reported in 49 cases. The spleen was described as palpable in 6 cases (12 per cent), and in 5 of these it was enlarged by weight (over 195 gm.) at autopsy. The largest spleen in the group weighed 1300 gm. and contained many tuberculomas in addition to miliary tubercles. Although 47 per cent of the spleens in this series weighed over 195 gm. at autopsy, only 4 (7 per cent) weighed over 400 gm., so that marked enlargement was rare both at physical examination and at autopsy.

Enlargement of the *liver* as a result of involvement in miliary tuberculosis is not usually described. Clinically, 35 per cent of these patients were reported to show palpable livers, but significant enlargement at autopsy was reported in only 6 per cent. In no case was it possible to demonstrate that hepatomegaly was due to miliary involvement of the liver per se.

Accumulation of serous fluids in amounts generally considered to be abnormally large was found at autopsy in many cases. Pleural fluid in amounts varying from 150 to 4900 cc. was found at autopsy in 19 cases (30 per cent) but was detected clinically in only 5 cases (8 per cent). Two cases in which no chronic tuberculosis of the lungs or pleura was found but in which diffuse pulmonary miliary tuberculosis was present showed significant amounts of fluid in the pleural spaces. Nine cases (14 per cent) showed abnormally large amounts of pericardial fluid at autopsy. In 5 of these, the amounts were relatively small, — from 50 to 75 cc., — and there were no symptoms during life attributable to the accumulation of fluid. In the other 4 cases, there was 150 to 800 cc. of pericardial fluid at autopsy. Two of these patients showed caseous tuberculous pericarditis before death. Miliary tubercles were found at autopsy in the pericardium in 2 cases, but in neither was there an abnormal increase in pericardial fluid. From 200 to 1500 cc. of intraperitoneal fluid was reported at autopsy in 4 cases (6 per cent), and the fluid was found clinically in 1 case.

Length of Hospital Stay and Duration of Disease

The shortest hospital course was twelve hours, and the longest was two hundred and twenty-five days. Seven patients died after being in the hospital for thirty-eight hours or less, and 6 remained there for three months or more. Most of the patients were in the hospital for two to four weeks. The length of the hospital stay and the duration of the disease are not, of course, necessarily synonymous. Most patients appeared to have developed the acute illness outside the hospital and to have sought hospitalization only when their symptoms became extremely severe. A few patients seem to have developed the condition while in hospital, and 1 patient suffered recurrent acute episodes, probably due to repeated miliary disseminations. In determining the apparent duration of the acute generalized miliary disease, such information was utilized as the onset of acute symptoms, the onset of febrile episodes, the changes in the leukocytes and x-ray information. Eighty-three per cent of the patients died two months or less after the apparent onset of acute symptoms, and the average duration of the illness was five and a half weeks. The shortest course in the series was five days in length, and the longest thirty-two weeks.

HEMATOLOGIC FINDINGS

Leukocytes

Adequate descriptions of leukocytic reactions in acute generalized miliary tuberculosis appear in the literature with some rarity. Warthin¹⁵ reported 2 cases in 1896 in which prolonged leukopenia and elevated percentages of neutrophils were found. As long ago as 1905, Arneith^{16, 17} pointed out that in this type of tuberculosis, as in the experimental

disease produced in animals by the intravenous injection of tubercle bacilli, it is the neutrophil that is most actively involved in the leukocytic reaction of the organism to the infection. He placed the emphasis on excessive demand for neutrophils rather than on defective supply in explaining the leukocytic changes. More recently, Medlar¹⁸ and Muller¹⁹ have expanded Arneth's views and have also directed attention to the important role of the neutrophil in tuberculous infection and to the demand made by local tuberculous lesions for such cells. The effects on the peripheral blood picture of such a demand seems to depend largely on the ability of the bone marrow to keep up with requirements. Thus, in any type of tuberculosis, if developing lesions make excessive demand for neutrophilic cells on the bone marrow, leukopenia may result. On the other hand, bone marrow response may be sufficient from time to time to produce frank leukocytosis. In either case many young neutrophils reach the circulating blood and the tendency for the count to shift to the left is more or less marked. That overwhelming infection, including tuberculosis, can at times produce what appears to be bone marrow depression is well known. There is no positive evidence, however, that the mere presence of miliary tubercles in the marrow can per se exert a depressant effect. In metastatic involvement of the marrow by neoplastic disease, Vaughan²⁰ found that the actual space occupied by neoplastic tissue was insufficient to account for the observed decrease in marrow function. Similarly, in none of our cases was there sufficient involvement of the bone marrow to allow explanation of peripheral blood changes on the basis of mechanical depression of marrow function. Interesting in this connection is the experimental work done by Doan and Sabin,²¹ who produced extensive lesions of the bone marrow in rabbits by intravenous injection of virulent tubercle bacilli. The result was initial depression of marrow function as judged by peripheral blood observations, followed in the animals that survived by compensatory hyperactivity of the marrow and finally by functional and morphologic recovery.

The increase in percentage of neutrophils and the more or less marked shift of the Arneth count to the left were stated by Arneth to be of definite prognostic and diagnostic value. Medlar¹⁸ considers, on the basis of numerous clinical observations, that in tuberculous patients an increase in the percentage and absolute number of neutrophils, whatever the total leukocyte count, is indicative of a progressive process. Such changes are not limited to acute generalized miliary tuberculosis but may be present in active pulmonary and other forms of active tuberculosis as well.

Our observations are based on 49 of the entire series of 63 cases. Eleven of the total number were excluded because of the presence of significant non-tuberculous infection at autopsy, 2 because no blood

counts were available, and 1 because of the presence of chronic myelogenous leukemia. So far as could be ascertained at autopsy, the 49 remaining cases showed no disease apart from the tuberculous infection that might have affected the blood picture.

Total leukocyte counts in the 49 cases were distributed as follows: in 24 cases (49 per cent) there was leukopenia (a total leukocyte count of less than 5000) at some point during the hospital course, in 14 cases (29 per cent) there was leukocytosis (a count of 10,000 or more) at some point during the hospital course, and in 16 cases (33 per cent) the total leukocyte counts were within the normal range. The highest total count was 20,700, and the lowest 1600.

In 11 of the 24 cases showing leukopenia at some time during the hospital course, the total leukocyte counts were persistently lower than normal for two weeks or more, the longest period of leukopenia being twenty weeks. In 6 cases, leukopenia, leukocytosis and normal total leukocyte counts were all observed. Seven patients showed leukopenia on entry but died before further observations could be made.

Differential leukocyte counts, like the total counts, varied in individual patients from time to time. A total of ninety differential counts was available in 35 of the 49 cases. Increased percentages of neutrophils, along with decreased percentages of lymphocytes, were observed in 31 cases (89 per cent). Immature neutrophils were extremely frequent, and in several cases the immature forms outnumbered the mature forms. In 4 cases there was an increased percentage of lymphocytes with a normal or slightly low percentage of neutrophils. Persistent monocytosis was not present in any case, although a slight increase in the percentage of monocytes was seen in thirteen of the ninety differential leukocyte counts available.

Of the 24 cases showing leukopenia, differential counts concomitant with low total leukocyte counts were available in 18. Fifteen of the 18 (83 per cent) showed an increase in neutrophilic elements, the highest percentage observed being 96. Immature neutrophils up to 25 per cent were observed in this group. Although 2 of the cases showing leukopenia also showed a slight decrease in neutrophilic elements, in none was there a picture consistent with or suggestive of granulocytopenia.

The combination of leukopenia and relative neutrophilia was striking. Although this combination, as indicated by Sturgis,²² is not limited to acute generalized miliary tuberculosis, it may be of diagnostic assistance. In typhoid fever, for example, the leukopenia is usually associated with relative lymphocytosis at the expense of neutrophils, and in true agranulocytic conditions the leukopenia is marked by extreme diminution of neutrophils and less marked diminution of lymphocytes.

Bone-marrow sections were made at autopsy in 37 of the 49 cases, and 33 of these contained miliary tubercles. The bone marrow in 19 of the 24 cases with leukopenia was involved by the miliary process and was uninvolved in 2 cases. No sections were available in the remaining 2 cases. In 9 of the 14 cases with leukocytosis, the marrow contained miliary tubercles, in 1 of the group no tubercles were present, and in 4 no sections were available. It is not surprising that no correlation between the hemopoietic activity of the marrow at the time of death and the blood picture during life could be es-

decrease in platelets and the resulting hemorrhagic diathesis. Armeth²⁷ reported extremely low platelet counts in 6 cases of this type of tuberculosis, all of which showed leukopenia and neutrophilia in addition. Two of our cases showed blood findings quite similar to those in Armeth's cases. The following points were common to both: moderate to severe leukopenia, with occasional normal or elevated total leukocyte counts, an increase in percentage of neutrophils, decreased platelets, normocytic or slightly microcytic anemia, and polychromatophilia. In addition, 1 case (Table 3) showed abnormal num-

TABLE 3 Summary of the Blood Findings in a Patient with Evidence of Myelophthisic Anemia

HOSPITAL DAY	WHITE-CELL COUNT	NEUTROPHILS		LYMPHO-CYTES	MONO-CYTES	NUCLEATED RED CELLS PER 100 WHITE CELLS	PLATELETS	HEMOGLOBIN (SAHLI)	RED-CELL COUNT	APPEARANCE OF RED CELLS
		MATURE	IMMATURE							
		%	%	%	%			%	$\times 10^6$	
1	5400	76		16	8		Decreased	72	3.8	
2	2800	76		20	3		Decreased	70	4.0	Moderate anisocytosis, MCHC, 32.3, and MCV, 83
3	4400	40	30	17	9	4	119,000	71	3.8	Moderate anisocytosis, polychromatophilia, MCV, 88.7, MCHC, 33.6, and MCH, 26.5
4	4000	48	27	12	8	4	Markedly decreased			
5	3400							68	3.7	
11	6000	60	14	18	7	3	Decreased	58	3.2	Anisocytosis and poikilocytosis
15	3800							61	3.0	
16								60	3.0	
23	4800	86		10	4	3	Decreased	55	2.8	Anisocytosis and poikilocytosis
29	2800							62	2.2	
32	6100						96,000	43	2.3	
37	5000	70		18	10	12	Decreased	46	2.3	Marked variation in size and shape polychromatophilia
42	5400							50	2.2	
49	8500	66		31	3	10		52	2.3	

established in the series. With regard to hemopoietic function, the bone marrow appeared normal or hyperactive in the overwhelming majority of cases, and definite hypofunction was noted in only 2 cases.

Hemoglobin and Red Cells

The occurrence of anemias of various types in pulmonary tuberculosis is discussed at length by Muller.¹⁹ Hegler³ gives the range of hemoglobin determinations and red-cell counts in acute generalized miliary tuberculosis as 65 to 85 per cent and 3,500,000 to 4,500,000, respectively. Both Hegler and Wintrobe²⁴ state that severe anemias in tuberculosis are rare.

In this series, 46 patients had both hemoglobin determinations and red-cell counts. Moderate normochromic anemia was seen in 39 (84 per cent). The lowest hemoglobin value and red-cell count were 43 per cent (Sahli) and 1,840,000, respectively. The vast majority of the determinations were well within the range given by Hegler.

Concomitant Depression of Blood Elements

The occurrence of a condition resembling so-called "aplastic anemia" in acute generalized miliary tuberculosis was noted by Dyke²⁵ and by Rosenthal,²⁶ the latter placing special emphasis on the

bers of nucleated red cells and increased numbers of immature neutrophils in the peripheral blood, findings consistent with the condition known as myelophthisic anemia and ordinarily associated with space-occupying lesions of the bone marrow. At autopsy the bone marrow contained relatively few miliary tubercles and showed markedly increased cellular density. There were signs of increased activity in both the erythrocytic and leukocytic series.

The second case of this general type in the early days of the hospital course showed a peripheral blood picture suggestive of an aplastic state. Blood studies done during this period all showed anemia, leukopenia and thrombocytopenia, and except for a slight to moderate increase in the percentage of polymorphonuclear cells, there was little peripheral evidence of compensatory activity on the part of the bone marrow. Subsequently there was steady improvement in the leukocyte picture, and when the patient died, four weeks after entry, a frank leukocytosis was in evidence. The appearance of the marrow at autopsy was in keeping with the findings in the peripheral blood in that there was increased granulopoiesis but decreased erythropoiesis. Miliary tubercles were present but were few in number.

PATHOLOGY

Pathogenesis

Since the original descriptions of acute generalized miliary tuberculosis by Bayle²³ and Laennec,²⁴ there has been considerable controversy concerning the pathogenesis of the disease. Much of this material has recently been reviewed by Auerbach.⁸

It has long been apparent that miliary disseminations are ultimately blood-borne. The condition is generally attributed to the release of relatively large numbers of tubercle bacilli, directly or indirectly, from a chronic focus, and it is about such foci that most of the controversy has centered. Laennec recognized a connection between a chronic tuberculous focus and miliary dissemination of the disease, a concept that was elaborated in some detail by Buhl¹⁰ in 1858. On the basis of autopsy findings, Weigert³¹ concluded that the disease stems from erosion and penetration of veins by extravascular tuberculous foci. Benda²² agreed in principle but suggested that tubercles of the venous intima, developing as a result of the lodging of a single bacillus or of several bacilli from the circulating blood, were ultimately responsible for the overwhelming release of organisms, resulting in acute generalized miliary tuberculosis. That a tuberculous lesion of the thoracic duct may initiate such a condition has also been postulated, and Hartwich¹⁰ states that such a lesion was apparently the origin of the miliary dissemination in 26 per cent of his cases. It appears from Auerbach's observations that chronic tuberculous foci, developing in lymphatic channels draining an infected area, ultimately break down and release tubercle bacilli into the venous circulation by way of the thoracic duct. This view is attractive from the anatomic standpoint, and it has in its favor the very extremely frequent involvement of lymph channels and lymph nodes draining chronic tuberculous foci.

Weigert's³³ tenet that chronic pulmonary tuberculosis renders the patient more or less immune to miliary disseminations can no longer be seriously considered. Auerbach's findings, as well as our own, are in complete disagreement with Weigert's statement on this point, since chronic pulmonary lesions were present in 64 per cent of his series and in 71 per cent of our own. Reisner³⁴ indicated the importance of chronic extrapulmonary foci, such as bone and genitourinary lesions, in the production of acute miliary disseminations, but in our series such foci were decidedly less frequent than pulmonary foci. Chronic pulmonary foci may give rise to chronic extrapulmonary foci, which in turn may originate acute miliary disseminations, and it is usually impossible to decide at autopsy which of the chronic foci was responsible for the acute episode.

A sudden release of large numbers of tubercle bacilli into the blood stream, whatever the site of origin, does not necessarily result in immediately

fatal disease. One of Auerbach's cases had four separate seedings of the lungs over a period of fifteen months, as demonstrated by x-ray and confirmed at autopsy. If, however, the number of organisms is large and the patient is unusually susceptible, the spectacular condition known as sepsis tuberculosa acutissima is said to occur. This condition is usually described as an extremely acute and generalized process that results in death before miliary tubercles have had time to form. At autopsy, small areas of necrosis containing numerous tubercle bacilli but provoking little or no cellular reaction are found scattered throughout the body. In addition to our 63 cases of acute generalized miliary tuberculosis, we noted 2 cases of chronic, healed miliary tuberculosis in which several disseminations had apparently occurred. No cases were found that could be classified as sepsis tuberculosa acutissima.

Criteria for Pathological Diagnosis

The establishment of suitable criteria for the pathological diagnosis of acute generalized miliary tuberculosis is far from easy. Our studies of the literature have failed to disclose any criteria that were entirely satisfactory. In practice, pathological diagnosis of cases in which the disease is truly overwhelming is not difficult. The difficulty arises when one attempts to decide just how generalized miliary involvement must be before a case may be labeled as acute generalized miliary tuberculosis. Clearly, the discovery of isolated miliary tubercles in a single organ does not justify the diagnosis, nor does the finding of numerous chronic but generalized lesions.

In selecting cases for a study of this type, one is unfortunately forced to establish definite criteria, even though dividing lines between various types of the disease are far from definite. We considered it essential to take the term "acute generalized miliary tuberculosis" literally so far as possible and made the following requirements for the pathological diagnosis: that the tubercles be acute, provoking little or no fibrous tissue reaction, that the disease be generalized sufficiently to involve the liver, spleen and at least one additional tissue, such as lung, bone marrow or kidney*, and that the tubercles conform, with regard to size, to the miliary description †.

Chronic Foci

The distribution of chronic tuberculous foci in this series is shown in Table 4. Chronic foci were found in 60 cases (95 per cent). The chronic lesions found in 45 of the cases (71 per cent) were all instances of fibrocaceous pulmonary tuberculosis. Intestinal lesions, present in 27 cases (43 per cent), were without exception chronic tuberculous ulcerations, and in 1 case the ulcerative process had pro-

*Three cases were included in which sections of liver or spleen were not available; numerous acute tubercles in four or more tissues other than these organs, however, were demonstrated.

†The size of the tubercles varies considerably, although most of those in our cases were 3 mm or less in diameter.

duced a spontaneous ileocolostomy. Distribution of the ulcerative lesions through the various portions of the intestine is shown in the table.

Chronic caseous lesions of lymph nodes were found in 37 cases (59 per cent). Infrequent examination of the thoracic duct probably accounted for the fact that this structure was found to be involved by chronic tuberculous lesions in only 4 cases.

Tuberculosis of the genitourinary tract, including the kidney, prostate, seminal vesicles, epididymis and testicles, occurred in 14 cases (22 per cent). Three cases in this group also showed tuberculous

TABLE 4 *Distribution of Chronic Tuberculous Foci*

LOCATION	No OF CASES	PERCENTAGE
Lungs	45	71
Lymph nodes	37	59
Tracheobronchial	26	
Mesenteric	14	
Abdominal	3	
Digestive tract	27	43
Esophagus	1	
Jejunum	7	
Ileum	23	
Colon	23	
Appendix	1	
Rectum	4	
Genitourinary tract	14	22
Kidneys	6	
Prostate	6	
Epididymes	4	
Testicles	1	
Seminal vesicles	2	
Adrenal glands	6	10
Spleen	6	10
Brain	3	8
Cardiovascular system	5	8
Heart	1	
Pulmonary arteries	2	
Pulmonary veins	1	
Ovarian vein	1	
Pericardium	4	6
Peritoneum	4	6
Bones	4	6
Thoracic duct	4	6
Pleura	3	5
Liver	1	
Pharynx	1	
Larynx	1	

meningitis, a finding apparently not in keeping with the frequent relation between tuberculous meningitis and tuberculosis of the genitourinary tract described by some authors.^{6, 7}

Chronic lesions of the cardiovascular system were seen in 5 cases. In 1 case, a caseous lesion of the tip of the right auricular appendage, measuring 0.9 by 0.5 cm., was found to have ulcerated through to the endocardial surface, at which point there was a small mural thrombus. Chronic lesions were found in the pulmonary vascular system in 3 cases—in the pulmonary artery in 2 and in a small branch of the pulmonary vein in 1. One of the lesions of the pulmonary artery took the form of a verrucous arteritis, and a fungating gray mass, approximately 0.7 cm. in diameter, was found attached to the intima 1 cm. above the pulmonary valve. Microscopically, the lesion contained numerous tubercle bacilli and cellular debris enmeshed in a fibrin network. Finally, there was 1 case of intimal tuberculosis of the ovarian vein.

Miliary Distribution

According to Auerbach,⁸ in cases in which miliary seeding is extensive, routine microscopic examination discloses miliary tubercles in almost all parenchymatous organs. Obviously, the number of organs routinely sectioned influences in large measure the apparent distribution of miliary lesions. Since the number of organs routinely examined varies considerably from laboratory to laboratory, many of the reported differences in miliary distribution are fictional.

Litten⁹ and most modern writers^{5, 8} state that the lungs, liver, spleen, kidney, bone marrow and choroid are always involved in acute generalized miliary tuberculosis and that the voluntary muscles are always spared. Miliary tubercles of the skin have been reported, but this finding appears to be extremely rare.³⁵

The miliary distribution in this series is presented in Table 5. The almost invariable involvement of

TABLE 5 *Distribution of Miliary Tubercles*

LOCATION	No OF CASES EXAMINED	CASES SHOWING TUBERCLES	PERCENTAGE
		NO	
Spleen	60	60	100
Liver	61	61	100
Bone marrow	50	42	84
Lungs	63	49	63
Kidneys	60	32	53
Adrenal glands	45	19	42
Testicles	12	5	41
Ileum	9	3	33
Meninges	24	7	29
Pancreas	25	5	20
Brain	24	3	12
Heart	39	4	10
Tracheobronchial nodes		13	—
Abdominal nodes		7	—
Peritoneum		7	—
Mesenteric nodes, urinary bladder, pleura, omentum, pericardium, jejunum and fallopian tubes		2 (each)	—
Epididymis, gall bladder, seminal vesicle, ureter, thoracic duct, duodenum, endometrium, ependyma, appendix, colon, pituitary gland, parathyroid gland and cervical node		1 (each)	—

the liver and spleen is well known. Our figures for these organs (100 per cent) may be artificially high, since the cases were selected on the basis of the finding of miliary tubercles in these sites. The extremely frequent involvement of the bone marrow has likewise often been pointed out. In the present series the bone marrow contained miliary tubercles in 84 per cent of the cases. Renal involvement by the miliary process occurred in 51 per cent, and the adrenal glands were diseased in 42 per cent. The latter figure is considerably higher than that found by Lewison et al.⁵ Although sections of the pancreas were made in only 25 cases, it is noteworthy that miliary involvement was found in 5 cases, a rather high incidence according to previous reports. Meningeal involvement was lower than is generally re-

ported, reasons for this discrepancy have already been mentioned. Miliary tubercles have often been noted in the thyroid gland, but in none of these cases was the gland examined. For the same reason, the frequency of involvement of the ocular choroid could not be determined.

DISCUSSION

From a practical point of view, more accurate diagnosis of acute generalized miliary tuberculosis is desirable for two reasons: first, the prognosis in the disease is considerably worse than that in most other forms of tuberculosis and may influence the physician's management of the case; second, more careful and detailed observations before death, particularly in the laboratory, may yield information of general value in tuberculosis.

The history often supplies no information of value, but may disclose either previous significant exposure to tuberculosis or the existence of chronic tuberculous infection. The incidence of acute generalized miliary tuberculosis among adults, particularly among those suffering from fibrocaceous pulmonary tuberculosis, was higher in this series than has generally been reported.

The course of the temperature is usually extremely irregular and is of little or no help in arriving at the correct diagnosis. More or less marked, sustained elevations of the respiratory and pulse rates may usually be expected. Although classification of cases of the disease into pulmonary and typhoidal types on the basis of temperature, pulse and respiratory charts figures prominently in the older literature, we doubt the justification for or clinical importance of such classification.

On physical examination, actual observation of miliary tubercles is possible only by ophthalmoscopic examination. We believe that a considerable number of our cases would have been correctly diagnosed before death had careful and repeated ophthalmoscopic examinations been carried out. Pulmonary findings in this series either were those of chronic pulmonary tuberculosis or were equivocal. Splenomegaly on physical examination occurred so infrequently that it was of relatively little diagnostic assistance. Spleen weights at autopsy sustained the finding at physical examination that pronounced splenomegaly in the disease is infrequent.

Among laboratory procedures the diagnostic importance of x-ray examination of the chest is fully established and needs no further comment. The importance of biopsy of the bone marrow as a laboratory procedure in the diagnosis of the condition was evidently not fully appreciated by the physicians in charge of our cases. Schleicher³⁶ has recently laid proper emphasis on this point and has described a method by means of which tubercles may be visualized in material obtained by marrow aspiration instead of biopsy. In view of the frequent involvement of the marrow at autopsy, it is apparent that

a definite ante-mortem diagnosis may be reached by ante-mortem examination of the marrow, a procedure that should certainly be resorted to in suspicious cases.

Serial examinations of the red and white cells appear to be of considerable diagnostic assistance, but isolated examinations are probably misleading as often as they are helpful. The most constant change in the leukocytic picture seems to be an increase in the percentage of neutrophils and a shift of the Arnett count to the left. These changes may be present whatever the total leukocyte count, but their diagnostic value is enhanced if they are found in association with leukopenia. None of these changes are specific for acute generalized miliary tuberculosis. When they are seen in patients known to be suffering from a chronic form of tuberculosis, the condition should be considered. If such a disturbance of the leukocytic picture develops in cases of obscure, febrile illness in which no specific bacterial agent is demonstrable, the disease should rank well up among the diagnostic possibilities.

Peripheral depression of several blood elements concomitantly, including leukocytes, red cells and platelets, is consistent with the diagnosis of acute generalized miliary tuberculosis but was not frequent in this series.

The chronic focus from which acute generalized miliary tuberculosis originates in a given case can seldom be definitely identified, but in the light of recent reports and of our own findings, we believe the lymphovenous route to be the likeliest one in the majority of cases, if not all. Chronic tuberculous lesions often develop in lymph nodes and channels draining an infected area. From this point, tubercle bacilli may easily enter the venous blood by subsidiary lymph channels and the thoracic duct. The latter structure may itself become incidentally infected, and less frequently it is involved from without by adjacent chronic lesions.

Many questions with regard to the distribution of miliary tubercles in acute generalized miliary tuberculosis remain unanswered. The frequent involvement of such sites as the liver, spleen, lungs and bone marrow is well established, but knowledge of the frequency of involvement of certain other sites is incomplete. Routine microscopic examination at autopsy of the ocular choroid, thyroid and pituitary glands, pancreas and adrenal glands in suspected cases would doubtless provide many of the answers not yet available. Our findings suggest that the adrenal glands and pancreas may be somewhat more frequently involved by the miliary process than is usually reported.

CONCLUSIONS

The general incidence of acute generalized miliary tuberculosis at autopsy among adults at the Boston City Hospital from 1937 to 1941, inclusive, was 1.55 per cent. The incidence of the condition among cases

of tuberculosis of all types at autopsy for the same period was 20.3 per cent

Although chronic pulmonary tuberculosis was diagnosed fairly accurately in this series, the clinical diagnosis of acute generalized miliary tuberculosis was achieved in only 25 per cent of the cases. The history and physical findings were of limited diagnostic assistance, x-ray examination of the chest and the clinical course being much more important in this respect. The only direct means of visualizing the miliary tubercles during life—namely, by ophthalmoscopic examination and bone-marrow biopsy—were grossly neglected in this series.

Splenomegaly was observed on physical examination in 6 cases (12 per cent), and the finding was confirmed at autopsy in 5. The spleen weighed over 195 grams at autopsy in 47 per cent of the cases, but enlargement by weight was marked (over 400 gm) in only 7 per cent. The average duration of life after apparent onset of the disease was five and a half weeks, the shortest course being five days and the longest thirty-two weeks.

Increased percentage of neutrophils and shift of the Arneth count to the left were present in 89 per cent of the 35 cases in which differential counts were made. Leukopenia was frequently seen but was by no means the rule.

Chronic tuberculous lesions were found in 95 per cent of the series. The lung was the site most frequently involved, being affected in 71 per cent.

The organs most frequently involved by miliary lesions were the spleen, liver, bone marrow, lungs, kidneys and adrenal glands. Some of the difficulties in establishing the frequency with which a given organ is involved by the miliary process are discussed.

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THE LATE RESULTS OF FEMORAL THROMBOPHLEBITIS AND THEIR TREATMENT*

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THE GROUPS OF LATE RESULTS

THERE is probably an advantage, in these recent days when thrombosis in the veins of the lower limbs is receiving active treatment by surgical procedures as well as by anticoagulants, in visualizing the usual end stage of the disease untouched by such methods. It is as yet too soon to learn how much or how little they alter its natural course, even supposing that in any considerable proportion of cases their use is attempted, for when one considers that venous thromboses occur in association with injuries, operations, childbirth and serious cardiac and other diseases, as well as spontaneously in everyday life, it is probable that in most instances today, the disease still has an opportunity to reach its full development.

In the light of present-day researches, culminating in the clinical observation of Bauer¹ and the pathological studies of Hunter and his associates,^{2, 3} it is clear that most venous thromboses begin below the knees. Undoubtedly they are then able to pursue a variety of courses, the nature of which has often been pointed out.‡ But how many undergo spontaneous cure, how many retain their character of soft thrombi likely to cause pulmonary embolism, and how many develop into the familiar, obstructive femorotibial thrombophlebitis is unknown. Certainly an obstructive, inflammatory thrombosis is the late stage toward which all such processes tend, and it is highly probable that it is by far the most frequent end result of all venous thrombosis in the lower limbs. I shall resist the temptation to show how surgical interruption of the diseased vein or the use of anticoagulants may modify or even prevent this development, and how, in the early stage of an actual thrombophlebitis, lumbar sympathetic block may favorably influence peripheral vasoconstriction and edema. These matters, of course, should sometime be studied in the light of the findings secured by such investigations as the present.

The late results of femorotibial thrombophlebitis seem to be divisible into five groups, and although some cases present features characteristic of more than one group, most of the 156 that form the basis of this report are easily classified. I have made no attempt to include the many patients I have seen in hospital wards, for these represent almost exclusively the disabling state of ulceration characteristic of Group 2. If included, they would still further enlarge that group.

Group 1 Some degree of edema remains, so that the ankle and lower leg swell during the hours of work or standing, discomfort is unimportant, congestion is not a feature, the skin is healthy, and the edema recedes, or even disappears, overnight. This group is large — how large is difficult to say, since many patients who fall into it make no complaints. I have included my own few cases, both for statistical purposes and for my brief account of treatment, with Group 2, for it is splitting hairs to isolate the mild edemas with negligible cutaneous changes from the serious ones complicated by pigmentation, induration and ulceration.

Since edema is the basic disorder in both groups, this is perhaps the best place to explain that it is likely to be due, not only during but after the acute stage of thrombophlebitis, to several causes — namely, elevated venous pressure, peripheral vasospasm (in the arterioles and venules) and impaired lymphatic drainage. These causes are so often combined that only occasionally is it possible to say that one of them alone predominates.

Group 2 Postphlebotic pigmentation and induration are present, and ulceration, in a variety of forms, often occurs. This group is far larger than any other. I find 95 cases, or 61 per cent, that fall into Groups 1 and 2. Edema is a constant feature. The typical lesion is usually referred to as "varicose ulcer," although varicose veins are seldom associated with it and, even if present, have no causal relation to it.

The characteristic physical signs are cutaneous pigmentation, diffuse induration, local heat and often ulceration, in the lower two thirds of the lower leg, usually on its inner face above the ankle. Sometimes this disorder is most marked near and below the malleoli, the inner rather than the outer. "Varicose eczema" is occasionally seen. There is thought to be present, according to Thompson's⁶ interpretation, a vicious circle of edema and sensitization of the tissues to foreign protein absorbed from the feet, toes and nail beds. The antigen is probably retained in the edema fluid for long periods.

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‡It is difficult to see why a soft and, at first, nonobstructive thrombosis should, in time, if it does not cause either fatal embolism or end in healing by local organization, go over to the obstructive, inflammatory type of disease. But Bauer has followed the process through, by phlebography, and one certainly encounters its earlier stages as betrayed by nonfatal embolism or local soreness, lameness (with or without swelling) and muscular irritability before the typical phlegmasia alba dolens sets in. Moreover, the pathological studies of Hunter, Sneed, Robertson and Snyder and of Hunter, Krygier, Kennedy and Sneed are consistent with earlier German and Swedish investigations in showing how frequently lower leg venous thromboses can be found in persons dying after confinement to bed by a great variety of diseases. One is thus made to realize that such thrombosis is common as a terminal affair and that it could readily go on to more advanced stages if death did not supervene. Again, Conner's⁴ account of prodromal signs in the legs and feet in the typhoidal thrombophlebitis of earlier days is strong evidence for early local lower leg thrombosis as leading to the full blown thrombophlebitis. I have attempted in a recent publication⁵ to picture diagrammatically the various courses that lower leg venous thrombosis may pursue.

of time. Actually, it appears to injure the walls of the arterioles, causing extravasation of blood, — hence the pigmentation, — and gives rise to a slow necrosis of fat with scar formation. Ulceration is not a primary feature. The source of the supposed antigen may be a fungus, — *Trichophyton*, — although in some cases it seems to be bacterial. In occasional cases, varicosity of the saphenous system, secondary to the original thrombophlebitis, contributes to the local disorder.

Group 3. A pain complex becomes established early in the convalescence and irrespective of all other signs. The situation and distribution of the pain have no relation to any of the great nerves. With it are usually associated vasomotor changes in the skin of the affected leg and a stocking-like paresthesia, the whole giving the impression of a functional disorder. This is a fair-sized group, there being 27 cases, or 17 per cent.

Group 4. The leg is the seat of marked venous congestion. The foot and ankle are usually involved, being slightly cyanotic with prominent surface veins. There may be distended veins on the abdominal wall and in the groin. Edema is not necessarily present, nor postphlebotic induration and pigmentation. This is the smallest group — 8 cases, or 5 per cent.

Group 5. Recurrent thrombosis occurs in the deep and, often, the superficial veins. This takes the form of attacks at varying intervals over a period of years. The attacks, because they usually involve veins previously thrombosed and canalized, are less outspoken than the original thrombophlebitis. They are an occasional source of recurrent, and therefore nonfatal, pulmonary embolism. This is a moderate-sized group of 26 cases, or 17 per cent.

TREATMENT

Although treatment is not of primary concern here, some account of what appear to be appropriate methods of managing the various groups is in order.

Groups 1 and 2. Since edema is the basic difficulty, it is obvious that its relief will cure early, mild cases and will favorably influence late, advanced cases, even though cutaneous and subcutaneous changes are well established.

The relief of postphlebotic edema is best initiated by a few days in bed, with the foot of the bed elevated 4 to 6 inches. Free exercise of the legs, to forward lymphatic drainage, is encouraged. This is a desirable introduction to any specific treatment.

If even a short, continuous stay in bed is impossible, at least the patient can sleep in a bed so elevated and can supplement such gravity drainage during the day by a number of ten-minute periods during which the leg is raised on an inclined plane to an angle of 20 to 30° and gently exercised. When going about or working, the patient should wear a semielastic bandage or elastic stocking from toes to knee, stand as little as possible and avoid sitting with the legs dependent and relaxed.

Hand in hand with the relief of edema goes treatment of the skin, intended to do away with sources of absorbed protein substances, chiefly derived from fungi. The nails must be softened by soaks, accumulations beneath them being gently scraped away. Partly depending on the acuteness or chronicity of such infections, soaks, liquid applications, ointments and powders may be used, a matter calling for expert dermatologic knowledge and technic. It is probably important that local applications should alter the reaction of the skin, in which direction it is not easy to say, but it is perhaps best in the direction of increased acidity.

Actual ulceration brings up the problem of secondary infection, possibly by anaerobic or facultative anaerobic bacteria, and calls for bacteriologic studies and the internal as well as the external administration of appropriate drugs. Only the ulcer not chronically infected will be cured by relief of edema and venous stasis alone. Should varicose veins be present, section or, rarely, excision should be used to relieve back pressure. Sclerosing injections seem always to do harm, in that they increase the local inflammatory reaction. Radical resection and skin-grafting of the diseased tissues should only occasionally be used.

Group 3. This group is characterized, as I have pointed out in an earlier publication,⁷ by a pain complex, and is distinguishable only by a history of thrombophlebitis from the "minor causalgia" that occasionally follows injury. It is, however, rather more responsive to treatment, and its identification is not difficult. The pain is "bursting" or "throbbing" or radiates down the center of the leg, being brought on, equally often, by exercise or long standing. The leg usually appears a little enlarged and, as a whole, faintly cyanotic, although dilated veins are absent. Below the knee, the skin is slightly "numb," — that is, dull to pinprick, — but distribution of the numbness does not follow the fields of the sensory nerves. Squeezing the calf as by a blood-pressure cuff, is very disagreeable. The peripheral pulses in the foot are sometimes diminished, — one of them may even be absent, — suggesting some degree of constriction of the large arteries.

Probably this state is residual from the vasomotor disorder of the acute stage of thrombophlebitis, for it is almost invariably relieved, for the moment at least, by sympathetic lumbar block. Successive reinforcing blocks prolong the period of relief and usually effect a cure. In late and obstinate cases, sympathectomy is required.

Group 4. This group, comprising the cases presenting venous congestion, yet with little or no edema, is one from which surgery has in the past been held to be barred, apparently on the ground that all distended veins, visible or invisible, are still capable of carrying blood uphill and must not be disturbed. This attitude should decidedly be recon-

sidered, no valveless veins draining the lower limbs—except the iliac veins and vena cava—are capable of forwarding blood against gravity, and since the column of blood they contain transmits high back pressures on lifting, straining and coughing, their interruption must always benefit and can never harm the venous return. Moreover, the blood that accumulates in, and even flows down, these veins must be carried by collateral vessels, which do the

back pressure. The canalization of thrombosed vessels is well known to pathologists, a process that I have illustrated in the accompanying diagrammatic sketches (Fig 1). The conditions pictured have actually been noted at operation. It would have been better if the veins had remained plugged, as Bauer,⁸ on phlebographic grounds, holds to be the rule.*

With these matters in mind, the femoral and saphenous systems of the congested postphlebotic

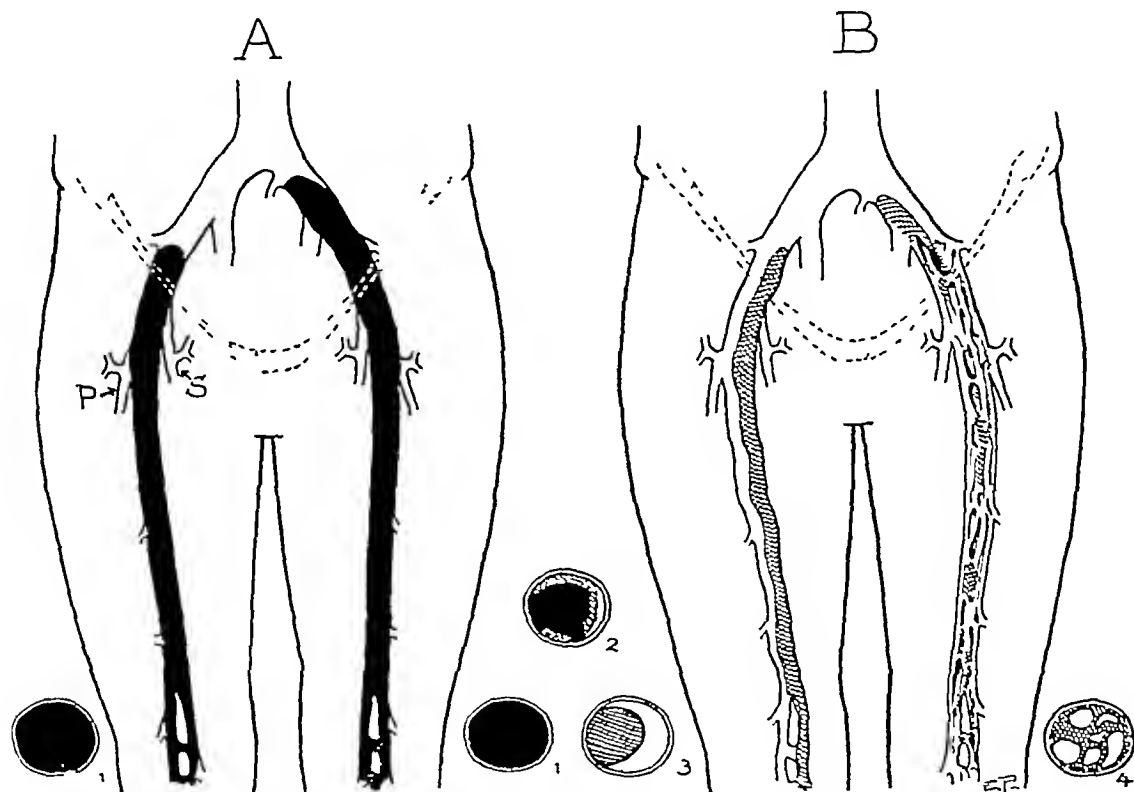


FIGURE 1 Semidiagrammatic Scheme of a Bilateral Obstructive Thrombophlebitis in the Lower Limbs

The process extends higher on the left than on the right. A represents the acute stage before organization, 1 and 1 being cross sections of the thrombosed femoral veins. B represents a later stage. In the right leg the thrombus has become a solid fibrous mass, shown in cross sections 2 and 3. In the left leg, the thrombus has been divided by multiple channels, shown in cross section 4. Both these conditions have been encountered on exploration.

work of the functionless veins. Presumably, the great veins sometimes seen in the groin and upon the abdomen of those who have suffered a long-continued plugging of the femoral and iliac veins are, in the acute stage of obstruction, the principal means of transmitting the venous return from the legs. Later, as alternative routes, by means of valved veins within the muscular envelope, are opened up, these overdilated veins become functionally useless. One can easily demonstrate the downflow of blood in all such vessels by the tests applicable to varicose veins in general.

The once thrombosed femoral vein itself must also be presumed to be a direct source of congestion and

leg may be studied and, if necessary, explored by a liberal incision in the groin. The saphenous vein should first be exposed and, if found diseased, divided at its point of entry into the common femoral. The femoral vein should then be inspected from this point downward for several centimeters—well below the entrance of the profunda femoris. It will usually be surrounded by scar tissue and will be

*Bauer's study of the sequelae of thrombosis takes up most thoroughly, many aspects of the problem but gives no descriptions of the actual state of the once thrombosed veins, as seen on section at the operating table or at autopsy. Moreover his phlebographic evidence that the veins superficial to the muscular envelope constitute the principal collateral pathways, ignoring the great intermuscular plexuses and their deep connections with the pelvis, is decidedly open to adverse criticism. Perhaps the superficial veins do offer the easiest way out for the venous blood when the patient lies flat as during phlebography but this does not mean that deeper vessels are not used in the erect position and during exercise.

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am going to go farther than Dr Homans and tell you what my experience has been in treating these cases. Long ago I was disturbed by seeing so many cases of obviously deep thrombophlebitis, characterized by thrombophlebitic ulcers without varicose veins, and with a history of repeated high saphenous divisions, without any obvious improvement in the ulceration.

As long ago as twenty-five years, Dr Homans suggested that the flap operation in the lower leg, with division of the perforating veins, might well be the answer. Dr Linton, I think, revived this idea, and suggested that these flap operations be more extensive, that they be done also in the lateral aspect of the leg, and that the appropriate perforating veins be divided. This does not seem to me to be sufficient. In addition, Dr Collier has suggested femoral divisions. This is not the answer.

Most of these cases, as Dr Homans has suggested, are associated, with reflex arterial spasm, which manifests itself by increased sensitivity to cold, increased sudomotor activity and the typical brawny edema and stiffness of the extremities, sometimes with atrophy of bone. I have come to believe that, after these patients have been subjected to procaine block, if they seem to improve, they should be immediately subjected to sympathectomy.

There is no doubt in my mind that patients who have had chronic thrombophlebitis have a tendency to develop recurrent thrombosis. If this is so, there is a grave danger of their developing a propagating thrombus and a lethal embolus. Heretofore my routine procedure has been to do a primary division of the superficial femoral vein, followed by lumbar sympathectomy. I have found that this is not enough, and have dissected the lower leg as well, doing a flap operation. Only by this method, I am sure, can one begin to salvage some of these unfortunate cases.

This seems like a great deal of surgery, but, as Dr Homans has mentioned, it makes little difference how much one divides these deep vessels so long as one does so high enough and

performs the subsequent operative procedures that clear up the lesions.

Concerning injections in postphlebotic legs, I mention them only to condemn them, because they are of no value and should not be done. This procedure is in the same category as dividing saphenous veins for deep thrombophlebitis.

Dr HOMANS (closing) I should like to say a word more about the pain complex, which fascinates me. Actually one does see it without other signs, in a leg that may look almost normal or show only a little bit of edema. Yet the patient makes a bitter complaint on having to stand a good deal and on taking exercise.

The most obvious things that one finds in going over a patient suffering from a pain complex are the peculiar, stocking-like paresthesia, which makes one think it is a hysterical affair, and the tenderness or soreness felt on compressing on the calf. These are the signs that mark this condition and the signs that are relieved, along with the pain, by blocking the sympathetic system. I have not paid so much attention as I ought to, perhaps, to the pain problem in the presence of other postphlebotic difficulties.

There is one matter that should not be slighted in treating these postphlebotic states, and that is the varicose veins that actually may develop, probably because of the dilatation that takes place while the main venous pathway is obstructed. One has to deal with these as one would deal with any varicose veins. It is well to have this in mind, but do not operate on a saphenous vein thinking you are going to cure the postphlebotic lesion. You may help it a little when the vein is obviously varicose, but the old idea of excising great areas of scarred and ulcerated tissue I have given up, probably because of increasing years. It is hard work and one does not get so much result from one's effort as one would like. Instead, a great deal can be accomplished by lessening the edema and treating the skin in the postphlebotic states, and thereby one is spared, and the patient is also, the labor and difficulty of some of these elaborate procedures.

DEXTROCARDIA AND BRONCHIECTASIS

A Review of the Literature and a Report of Two Cases

A. H. RUSSAKOFF, M.D.,* AND HARVEY W. KATZ, M.D.†

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IN THIS decade of increasing mass radiography, when the United States Public Health Service, state health departments, tuberculosis associations, private industries and other agencies are interesting themselves in x-ray survey programs, it is not amiss to call attention repeatedly to nontuberculous diseases of the chest. In most cases during the conduct of chest x-ray surveys, persons who are found to have such abnormalities are referred to their private physicians — not to specialists — for further investigation. Consequently, it is incumbent on progressive physicians to become well versed in the roentgenographic as well as the other aspects of diseases of the chest. Although no disease of the chest constitutes a public-health problem of the magnitude of pulmonary tuberculosis, others are of paramount importance to the health, welfare and livelihood of those persons concerned.

The purposes of this paper are to report 2 cases of dextrocardia and bronchiectasis, to call attention to

this clinical entity among nontuberculous diseases of the chest, which will be recognized more frequently during the ensuing years and to present evidence that transposition of the viscera is attended by a high incidence of other significant abnormalities.

The coincidence of bronchiectasis and dextrocardia was first reported by Siewert¹ in 1904. From that time until 1933, only 2 additional cases appeared in the literature.²⁻³ At that time, in recording 4 cases, Kartagener⁴ observed the coincidence of sinus disease in association with bronchiectasis and visceral transposition. The simultaneous occurrence of these three conditions has been termed "Kartagener's triad." Kartagener, who was a proponent of the theory of the congenital origin of bronchiectasis, maintained that these cases lent proof to this tenet. In 1935, Kartagener and Horlacher⁵ reported 7 additional cases, which were found in several European clinics.

Two years later, Adams and Churchill⁷ published the first paper in the English language on this subject. Among 23 cases of situs inversus, they found 5 with bronchiectasis. A review of embryologic data

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whitish, instead of its usual blue color. Often the heavy scar of the organized thrombus can be felt, the vein being a solid-feeling cord, which, however, is actually distensible. In the figure, the state of the femoral and iliac veins, as I have seen them on section at the operating table, is diagrammatically pictured. Whether I am right in believing that the canalizing process is as complete as I have suggested may, of course, be questioned. In any case, the vein that I have described is functionally useless and can be divided with impunity.

Far from aggravating the signs of venous stasis, a common femoral or iliac division results in lessened distention of the superficial veins and an improved color of the foot. Any edema that is present may be diminished, although edema and its complications are less likely than venous congestion to be relieved, as Collier and his associates^{9, 10} have reported in studying the results of femoral-vein interruption. Their indications are mainly chronic induration and ulceration, rather than the venous stasis that I have described here, and the recurrent thrombosis described under Group 5.

If distended veins on the pubis and abdominal wall are proved to be functionless, they may be reduced in number and size by section and perhaps injection, but although my experience indicates that their obliteration does no harm, it has also shown that it is even more difficult to make permanent than is the case with varicosities of the legs.

Group 5. Cases of recurrent thrombosis, with or without embolism, naturally present no consistently abnormal appearances. The affected leg usually shows some of the aftereffects of the original thrombophlebitis. Pulmonary infarcts rarely recur without other evidence of old or fresh thrombosis, in which event it must be supposed that a thrombus forming in a canalized, useless vein is locally silent. I have a record of one such case, in which repeated pulmonary infarction simulated angina pectoris and the patient had been made an invalid.¹¹ Section of the external iliac vein prevented further recurrence. On division of the vein, ribbonlike masses of scar tissue were noted, much like those shown in the figure.

In other cases, there has been a history of recurrent swelling and lameness of the calf. In yet others, small superficial local thromboses have pointed very strongly to the presence of a deeper process, of which they are merely a complication.

Although section of the common femoral vein must often serve, the ideal treatment for all such recurrent thromboses is ligation of the corresponding common iliac vein, because this high division secures the best collateral venous circulation and gives the greatest help in the prevention of future thrombosis and embolism. Unfortunately, a previously, and perhaps repeatedly, thrombosed common iliac vein is difficult and sometimes dangerous to deal with, for it is frequently found to be both adherent and

fragile, requiring the greatest care in handling. Ligation of the vena cava may even be required.

SUMMARY

On the reasonable presumption that femoriliac thrombophlebitis is the usual end stage of thrombosis in the deep veins of the leg, an attempt has been made to group the various abnormal states that follow such a thrombophlebitis. Five groups of patients have become distinguishable among the ambulatory persons who present themselves as office patients—namely, those characterized, respectively, by edema, by edema plus induration, pigmentation and ulceration, by a pain complex, by venous congestion and by recurrent thrombosis.

These groups overlap, yet by a study of the clinical history and physical signs, every patient can be placed, for purposes of treatment, in one group or another.

Appropriate means of treating the members of each group are suggested.

It will be a matter of great interest to discover how modern treatment, especially of the earlier stages of venous thrombosis in the lower limbs,—that is, by operation and anticoagulants,—influences the establishment of femoriliac thrombophlebitis and its late results.

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DISCUSSION

DR. E. EVERETT O'NEIL (Boston): This is a new grouping of cases that Dr. Homans has outlined, and for anyone who sees a large number of these conditions, it is an excellent working formula. The second group that he mentioned, which manifests itself by a tremendous amount of induration and ulceration and scarring in the lower inner third of the leg, represents what is probably one of the most difficult venous conditions with which the surgeon has to deal. This problem has engaged my interest for several years.

The third group mentioned, in which pain alone is an outstanding phenomenon, has not in my experience been observed alone. It is usually found, so far as I am concerned, in conjunction with the other phenomena of ulceration, induration and scarring.

So far as the treatment of the second group is concerned,—and to me this is the most important of the five groups,—I

found that 1.13 per cent of 442,252 persons examined in surveys showed some type of significant nontuberculous aberration. Of the entire group, 0.6 per cent had abnormal hearts, whereas 0.009 per cent (approximately 1 in 11,000 persons examined) had dextrocardia. Scatchard and Duszynski²⁴ reported 1 case of dextrocardia in 2721 roentgenographic examinations in a general hospital. Morse²⁵ found 36 cases among 223,182 examinations, a frequency of 1 in 6200. Russakoff²⁶ has observed 6 cases among 36,717 persons examined in surveys, a frequency of 1 in 6120.

Olsen⁸ in reviewing the files of the Mayo Clinic from 1920 through 1941 found 85 cases of dextrocardia. Of these, 14 were discovered to have an associated bronchiectasis, an incidence of 16 per cent. During this identical period a diagnosis of bronchiectasis was made on less than 0.5 per cent of all other patients investigated. Thus, the frequency of bronchiectasis in this series was thirty-three times as great among persons with dextrocardia as among a representative clinic population. Kartagener and Horlacher⁵ found 23 per cent of their patients with dextrocardia to have bronchiectasis, and Adams and Churchill⁷ found this correlation to exist in 22 per cent of their group. It is interesting to note that Morse²⁵ reported 1 case of bronchiectasis in his group. His study, however, deals only secondarily with cases of dextrocardia, and it is therefore assumed that a complete study for bronchiectasis in all cases was not made.

Although it may justifiably be argued that the true incidence of bronchiectasis in a representative clinic population is probably in excess of 0.5 per cent, it is still undeniable that the coincidence of bronchiectasis with visceral transposition is unusually high. Thus, the obvious conclusion to be drawn from these studies is that the consistently high incidence of bronchiectasis among patients with dextrocardia is hardly to be explained as a chance occurrence.

Dextrocardia is altogether too frequently considered to be an anomaly of little if any significance, yet Olsen⁸ observed that 11 of his patients, exclusive of those with bronchiectasis, had additional significant defects and 2 others had cardiospasm. Thus, of 85 persons with dextrocardia, 32 per cent had other significant abnormalities.

* * *

These observations obligate physicians to adopt a somewhat different attitude toward cases of dextro-

cardia. It is no longer sufficient to inform the patient of transposition of the abdominal viscera in cases of situs inversus to avert the catastrophes of improperly interpreted contralateral abdominal manifestations. Besides a search for other anomalies, a thorough investigation of the upper respiratory system and the bronchopulmonary tree should be an integral part of a complete clinical study. Bronchography should perhaps be performed with less conservatism in such cases than is practiced among patients without dextrocardia.

With recognition of the fact that more cases of dextrocardia are bound to be uncovered in practically every community as a byproduct of mass radiography in the control of tuberculosis, it is timely that physicians take cognizance of the high incidence of significant abnormalities associated with this condition.

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led them to conclude that the bronchiectasis in these cases represented a stigma of maldevelopment. In 1943, Olsen⁸ reported 14 cases of bronchiectasis among 85 patients with dextrocardia. This is the largest single group of cases reported to date.

Besides the reports already mentioned, the following are noted: Nüssel and Helbach's⁹ 2 cases and single case reports by Behrmann,¹⁰ Casaubon and Derqui,¹¹ Wernli-Haessig,¹² Glaum,¹³ Becker,¹⁴ Rosenthal,¹⁵ Ingraham,¹⁶ Cole and Nalls,¹⁷ Nagy,¹⁸ Adland and Einstein,¹⁹ Meyer,²⁰ Richards²¹ and Delp.²² Including the 2 cases that follow, there are 50 cases of dextrocardia and bronchiectasis on record.

CASE REPORTS

CASE 1* L M O, a 34-year-old man, was admitted to the Bryce Hospital, Tuscaloosa, Alabama, in 1934 with a diagnosis of mental deficiency and psychosis. In the past he had been subject to frequent respiratory infections and severe sore throat. The family history was noncontributory. On examination the patient was found to be dull and childish. He coughed frequently, producing foul, yellow, tenacious sputum. The significant findings were as follows: a deviated septum with both nares occluded by a mucopurulent discharge, dental caries and fetor oris, diffuse injection of the pharyngeal mucous membrane with copious postnasal drip, palpably enlarged lymph nodes in the anterior



FIGURE 1 Case 1

cervical chain, dextrocardia with no enlargement, arrhythmia or auscultatory abnormality, an admixture of dry and moist rales over both lower lung fields, and evidence of transposition of the abdominal viscera.

Additional studies included a conventional radiogram of the chest, which demonstrated the dextrocardia. The bronchial markings into both lower lung fields were decidedly

exaggerated, and there was evidence of peribronchovascular inflammatory change. Bronchography of the right lower lobe (Fig 1) showed a cylindrical type of bronchiectasis. A plain film of the sinuses demonstrated a bilateral chronic frontal and maxillary sinusitis.

CASE 2 P S, a 7-year-old girl, is the private patient of one of us (H W K). The prenatal history and delivery were uneventful. Within 24 hours after birth the infant had cough and cyanosis. X-ray examination of the chest at that time revealed dextrocardia, without parenchymal change. There was subsidence of the cough and cyanosis within a few days. The patient had had a chronic cough productive of a mucoid expectoration since early life. When 4 years of age, she received tonsillectomy and adenoidectomy. Following this procedure, it is believed that the cough became less productive. At 5 years of age, the patient had an uncomplicated case of chicken pox. For years the patient had had frequent

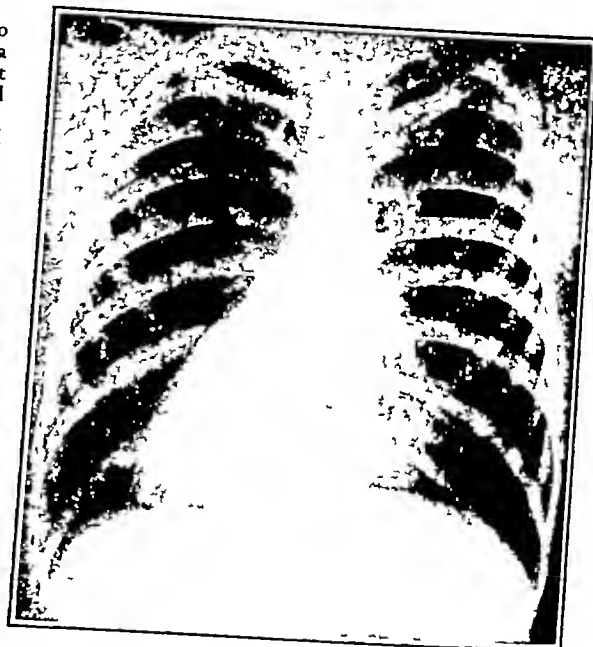


FIGURE 2 Case 2

upper respiratory infections, associated with rhinorrhea and postnasal discharge. During the year previous to examination, a diagnosis of sinusitis was made by an ear, nose and throat consultant.

On physical examination, the patient was found to be well developed. There was no evidence of cardiorespiratory distress, although there were a frequent moist cough and questionable cyanosis. Significant physical findings were dextrocardia, with no enlargement, arrhythmia or murmurs, moist and dry rales over both lower lung fields posteriorly and transposition of the abdominal viscera.

A conventional posteroanterior radiogram of the chest showed the dextrocardia to be associated with a generalized increase in the bronchial markings. On the left side, the cardiohepatic angle was obtunded by soft flocculent shadows. In the right lower lung field, there was evidence of peribronchovascular inflammatory change.

Lipiodol was instilled into the right lower lung field by Dr. Robert M. Lowman, radiologist of the Grace Hospital, New Haven, Connecticut. Under fluoroscopy a cylindrical dilatation of the second and third dorsal bronchi could be visualized (Fig 2).

One of the valuable byproducts of mass radiography in the control of tuberculosis is the detection of nontuberculous pulmonary disease. Gould²³

*This case is reported with the permission of Dr. W. D. Partlow, superintendent of the Bryce Hospital. It was correctly diagnosed on 35 mm film, being discovered during the conduct of a survey for tuberculosis.

formerly. Hence present control of diphtheria must be concerned not only with immunization of a wider age group than previously but also with the necessity of maintaining immunity once it has been established. In the application of procedures under these circumstances, several points deserve particular consideration.

Choice of immunizing agent. The antigenic superiority of toxoid over toxin-antitoxin has long been established¹⁸⁻²⁰. When the slight though real dangers of serum sickness from toxin-antitoxin²¹ and the inherent risk of administering a toxic preparation²² are also considered, there appears little justification for its continued use except under special circumstances. The principal choice thus narrows down to FT (fluid toxoid) versus APT (alum-precipitated toxoid). Both, when properly used, are extremely effective as judged by the production of a negative Schick test. Fraser and Halpern²³ and Volk and Bunney²⁵ found that about 95 per cent Schick reversals may be observed a few months after administration of two doses of APT or three doses of FT. It is possible that APT is slightly superior to FT, but the difference is considerably less than can be observed, for example, between good and poor batches of APT.^{9, 26, 27} The experience of recent years suggests that occasional or perhaps periodic reinforcing doses of toxoid are required to replace the stimulus no longer provided by the diphtheria carrier. Such repeated doses increase the possibility of allergic reactions to constituents of the toxoid, and it has been variously demonstrated²⁸⁻³⁰ that alum precipitation markedly enhances the capacity of toxoid and other antigens to produce reactions of hypersensitiveness. Thus, Fraser²⁴ warns against the possibility of obtaining undesirable anaphylactic reactions when immunity is reinforced by a subsequent dose, since APT is extremely effective in rendering guinea pigs sensitive and anaphylactic, the administration of a second or subsequent dose at long and irregular intervals may increase the danger of such reactions in man. Additional objections raised against APT are the greater frequency of local reactions,³¹⁻³³ the localization of smallpox vaccination at a site recently injected with APT³¹ and the difficulty of maintaining a uniform suspension, particularly in mass immunization.³⁴ It should be noted, however, that allergic reactions to APT are extremely rare and that studies suggest that similar reactions to tetanus toxoid can largely be ascribed to the presence of an obsolete ingredient in the medium rather than to the bacterial protein itself.³⁵ Moreover, APT has the definite advantage of requiring only two instead of three doses for adequate primary immunization. This may therefore prove to be the agent of choice wherever geographic, educational or administrative factors make it difficult to ensure completion of three doses, whereas FT may be preferred wherever the completion of a three-dose schedule

presents no major problem. With either agent, it should be possible to obtain a toxoid free of antigenic constituents other than those caused by the diphtheria bacillus itself, since Mueller et al.³⁶⁻³⁸ and others³⁹⁻⁴¹ have demonstrated that a potent FT or APT can be produced on a peptone-free medium. Such a medium has been used for the entire production at the Massachusetts Antitoxin and Vaccine Laboratory for over six years.

Preferred dosage and interval. There is no longer any justification for attempting immunization with one dose of APT or two doses of FT except in an emergency, although these inferior methods give better results than no immunization.^{42, 43} Both systems have had their vogue, and both are now generally discredited as being insufficient to produce an adequate, sustained immunity,^{24, 25, 43, 44} although Bousfield^{45, 46} and others maintain that, when diphtheria is prevalent, adequate results may be obtained with one dose of APT. The recent description of a diphtheria outbreak among a group of children, most of whom had received one dose of APT,⁴⁷ and similar experiences⁴⁸ testify that such a procedure does not protect effectively against intimate exposure to virulent bacilli. Proper immunization, therefore, is still based on two doses of APT or three of FT. Likewise, proper immunization depends on spacing the doses at least three weeks apart, regardless of which agent is used. The practice of giving successive doses of APT one week apart seems never to have arisen, but it is still widely supposed that an interval of a week is sufficient when FT is used, despite Ramon's⁴⁹ evidence to the contrary many years ago. Numerous recent studies have shown that a longer interval is also advantageous when APT is used.⁵⁰⁻⁵² Furthermore, experience with tetanus toxoid, pertussis vaccine, typhoid vaccine and other immunizing agents points to the advantages gained by lengthened intervals between doses.

Various British studies on APT immunization have recently reopened the question of the optimal size of dose.^{9, 26, 27, 45, 53} The evidence suggests that doses as small as 0.1 to 0.3 cc. are effective.⁹ These studies were for the most part carried out in areas where diphtheria was more prevalent than in the United States, also the subjects were not followed up with Schick tests later than four or five months after immunization. The results must therefore be re-evaluated before they can be judged in the light of American conditions and standards.

Results obtained with toxoid. As suggested above, the results obtained vary with many factors, among the most important of which is the interval between immunization and follow-up. Fraser and Halpern⁵⁴ have shown that three months after immunization with three doses of FT, a large number of previously susceptible children had over 0.02 unit of antitoxin per cubic centimeter of serum, this is more than five times the amount necessary for the production

MEDICAL PROGRESS

ACTIVE IMMUNIZATION

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THE continued extension of public-health and preventive medical activities, the need for new and massive immunization programs among the armed forces of the United States and other countries, and the corresponding impetus that the war gave to investigations concerning active immunization have in recent years produced an enormous mass of theoretical and experimental observations in this field.

In this review no attempt is made to cover any branch except active immunization as it applies to diseases existing in New England for which such immunization is of practical interest—that is, diphtheria, scarlet fever, tetanus, pertussis, typhoid fever, smallpox, influenza and rabies. Even within this range, the review is essentially incomplete, in so far as it omits many subjects that are now primarily of theoretical interest but on which important future trends in active immunization may depend. Such topics as the mechanisms of immunization, the immediate and late effects of hypersensitization and their underlying mechanisms, the so-called “interference phenomena” that have recently come to light—especially in the field of virus infections—and the significance of nonspecific protein reactions (among which may be included the recently publicized antireticular cytotoxic serum of Bogomolets¹) are inseparably related to active immunization but, for practical reasons, cannot be considered.

All the commercial laboratories and several of the larger state and municipal laboratories preparing biologic products for immunization operate under licenses from the Federal Security Administration, through the National Institute of Health of the United States Public Health Service. Such laboratories, which are regularly inspected by officers of the National Institute of Health, must, with few exceptions, submit samples and protocols of each batch of the product distributed, must clearly label the package in certain specified respects and must conform to certain minimum requirements governing safety and, generally, potency. Consequently, one may be reasonably certain that such products are not harmful and that, so far as practicable, their effectiveness is maintained above a specified minimum. Beyond these limits, however, the National Institute of Health recognizes that large areas exist

within which possible improvements in methods of production, testing and use may be found. Currently, continuing studies of all types of research, as well as extensive applications of biologic products to human patients by clinicians and public-health workers, guarantee that no product or method will remain static for long. Moreover, since epidemic disease knows no artificial boundaries, the advances in this field have been world wide, the material presented below has accordingly been drawn from almost as wide a range as the scope of the diseases in question.

Several general textbooks and reference books published in recent years have given considerable space to the preparation or the use of biologic products.²⁻⁶ Such texts are of great value for general information and reference. Each includes primarily topics of particular relevance to the text, and therefore each must be supplemented with data from other sources, to cover wider areas as well as to bring the information contained up to date. Current advances in the related subject of diagnostic skin tests have recently been reviewed.⁷

DIPHTHERIA

The decline in the diphtheria case and death rates, which began many years ago, has been greatly accelerated by the use of artificial immunization, so that within the last few years case rates of less than one hundredth of those sixty years earlier have been recorded, as in Massachusetts.⁸ This decrease has been accompanied by a tremendous decline in the carrier rates in artificially immunized communities, and hence in the frequency of naturally acquired stimuli to immunity, in turn apparently related to a widely noted decrease in the general level of immunity in certain sections of the population. Schick-test surveys among young adults or adolescents in England, Canada, Australia and the United States have shown that 50 to 60 per cent are susceptible to diphtheria,⁹⁻¹⁶ in contrast to the incidence of 20 to 25 per cent of positive reactions formerly reported in these age groups.¹⁷ Thus a growing reservoir of young adults susceptible to diphtheria appears to exist. A parallel consequence of the reduced prevalence of diphtheria bacilli is that artificially induced primary immunity is likely to wane and disappear more rapidly than

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of infants whose mothers are not immune. Where diphtheria is prevalent, its occurrence in infants represents a real danger, for it can readily produce an atypical and overwhelming infection.⁹⁶ Liebling, Youmans and Schmitz⁹⁷ have offered a partial solution to this problem by antenatal immunization of Schick-positive mothers. A small group whose response was followed beyond the neonatal period, however, indicated that the immunity thus transferred to the infants was even shorter lived than the inherited natural immunity.⁹⁸

Combined immunization with diphtheria toxoid and other agents is discussed below, under tetanus, pertussis and typhoid fever, since such combinations are usually designed to incorporate other agents into an established procedure for diphtheria immunization.

SCARLET FEVER

The many factors involved in the medical and administrative control of scarlet fever have recently been thoroughly reviewed.⁹⁹ There is fairly general agreement that streptococcal toxin prepared, standardized and used according to the methods prescribed by the Dicks¹⁰⁰ prevents the development of clinical scarlet fever in a great majority of persons exposed. In this respect Anderson's¹⁰¹ review of a decade ago is fully valid today. Place,¹⁰² Lucchesi,¹⁰³ Toomey¹⁰⁴ and others have confirmed the numerous earlier reports that immunization according to the Dick method practically abolishes the occurrence of scarlet fever among nurses working in contagious wards. Graham¹⁰⁵ reports that follow-up Dick tests were negative in 86 per cent of 50 private patients tested five to ten years after immunization, and in 84 per cent of 30 subjects thirteen to fifteen years after inoculation. Little¹⁰⁶ observed 63 cases of scarlet fever among 6982 immunized subjects observed over a seven-year period, in contrast with 915 cases among 8063 unimmunized persons — an attack rate of 0.9 per cent in the former as against 11.3 per cent in the latter.

Such an effective procedure would have been universally accepted long ago if it did not have definite drawbacks. Foremost among these are the frequency and severity of the reactions produced by the dosage of the subcutaneous injections of toxin recommended by the Dicks, which are usually 650, 2500, 10,000, 30,000 and 100,000 to 120,000 STD (skin test doses) at weekly intervals. There is still, as Anderson stated,¹⁰¹ surprising unanimity of opinion regarding the severity of reactions to toxin injections, most observers mentioning severe reactions in as many as 10 or 15 per cent of cases. Jacobs and Orris¹⁰⁷ report an incidence of 28 per cent of moderate or severe reactions, including nausea, vomiting, fever and a rash comparable to that of mild scarlet fever itself. Less frequent, but perhaps highly significant, is the occurrence of joint manifestations,¹⁰⁸ which have been found to exhibit

a high degree of association with a history or signs of rheumatic fever. Such a relation possibly explains the reported fatal reaction occurring in a thirteen-year-old boy following an initial 500 STD of scarlatinal toxin.¹⁰⁹ At all events, it becomes difficult to justify the widespread use of a procedure that may cause reactions such as those described. Moreover, there is considerable doubt whether the scarlatinal rash is produced by only one antigenic type of toxin.¹¹⁰ Hence, with the various factors concerned taken into consideration, it has been authoritatively stated that information is at present sufficiently convincing to render immunization against scarlet fever as a routine or community-wide practice under official auspices inadvisable until a more suitable antigen becomes available.¹¹¹

Nevertheless, certain groups must be immunized, particularly physicians, nurses and ward attendants likely to come in contact with cases of scarlet fever. Also the relatively high incidence of susceptibility among young adults, as evidenced by the Dick test or by clinical experience, can be of serious concern to military establishments and in civilian communities during high prevalence of the disease. Many attempts have therefore been made to overcome the difficulties encountered with the standard immunizing procedure by modifying the dose, the administration route or the antigen itself. Howie¹¹² employed a dosage schedule widely used in Canada (330, 1000, 2300, 5000 and 10,000 STD) in the immunization of over 8000 school children at the onset of an epidemic of scarlet fever in Windsor, Ontario, five months later, 89 per cent of a representative sample of the group were Dick negative, and statistical data indicated that the epidemic had been checked, in contrast to the neighboring city of Detroit, where it continued unabated. Glazier¹¹³ immunized 340 children over a period of years with seven weekly doses of 650, 2500, 5000, 10,000, 25,000, 55,000 and 110,000 STD respectively, reactions occurred after only 7 per cent of the injections, and Dick tests (one week after the last dose) were negative in 265 out of 268 children tested. None of the 340 patients subsequently developed scarlet fever.

Others have tried intranasal, percutaneous, intracutaneous and oral administration of the toxin, Graham has reviewed most of these studies.¹¹⁴ The intracutaneous route has given excellent early results in some hands,¹¹⁵⁻¹¹⁸ although as many as ten doses were required in individual cases to produce a negative Dick test.¹¹⁷ Late follow-up Dick tests, however, indicated that a large number of the patients had reverted to the Dick-positive state.^{107, 117} As indicated elsewhere, there is increasing reason to believe that the intracutaneous route is probably not dependable for routine primary immunization, although it can doubtless be used successfully in carefully handled individual cases. Results with the percutaneous, intranasal and oral routes, including 59 of Graham's patients given toxin intranasally, in-

of a negative Schick test,⁵⁵ which in turn is generally correlated with resistance to diphtheria.⁷ A year later 3 per cent and three years later 8 per cent of the group were Schick positive, whereas five years later 34 per cent had reverted to the Schick-positive state, and the average serum antitoxin titer was only 20 per cent of the maximum obtained shortly after immunization.⁵⁶ A more recent study indicates that among young adults the relapse rate may be as high as 20 per cent in one year.⁵⁷ Thus, the protection against diphtheria observed in any large group decreases in proportion to the interval since inoculation. Nevertheless, the clinical protection afforded by toxoid immunization is impressive. With few exceptions⁵⁸⁻⁵⁹ the incidence of diphtheria among immunized persons averages about 10 to 15 per cent that among nonimmunized controls.^{43, 60-62} Moreover, diphtheria is usually milder in inoculated than in unimmunized persons.⁶²⁻⁶⁶ Occasional cases occurring in previously immunized patients, however, sometimes arouse doubts concerning the efficacy of immunization in general, it is only by adjustment of the observed case rates to the relative numbers of the immunized and unimmunized persons, as Gibbons⁶⁰ has done, that the high degree of protection actually achieved by immunization is made clear.

Immunization of adolescents and adults with toxoid In virtually all the usual immunization programs, diphtheria toxoid is the only agent used. The provision of toxin-antitoxin mixture in Massachusetts for group immunization is being continued temporarily because of long familiarity with this agent — particularly for adult immunization — and the admitted difficulties arising from the relatively frequent reactions experienced by adolescents and adults receiving toxoid in the routine dosage. Extensive experience in Canada and several states in this country, however, indicates that reactions can largely be avoided by the inoculation only of persons who are Schick positive, the performance of the Moloney test, using 0.1 cc of diluted toxoid, on the Schick positives⁶⁶⁻⁶⁸ and the administration of divided doses of toxoid or diluted toxoid to subjects showing positive Moloney reactions.⁶⁹ The usual initial dose in older subjects is 0.1 cc^{70, 71} which has in fact on occasion been substituted for the Moloney test.^{72, 73} Recent observations suggest that immunization should be withheld from persons exhibiting any reaction to the Schick control test,¹⁶ which should therefore always be employed in subjects tested in these age groups, since such reactors almost always possess either actual⁵⁵ or latent¹⁶ immunity and usually show marked reactions to toxoid.⁷⁴ Furthermore, Wishart et al.⁷⁵ and Paschlau⁷⁶ have noted a direct correlation between severity of reaction and degree of immunity, so that in group immunizations one may safely leave the toxoid reactors with a single stimulus from the Schick or Moloney test,

or both. This principle has been followed on a large scale in military establishments.⁷²

Other immunization routes Numerous workers have experimented with intranasal immunization with toxoid by drops⁷⁷⁻⁸⁰ or sprays.⁸¹ As a procedure for primary immunization, the intranasal route appears less potent than the parenteral, whereas its use for reimmunization is likely to lead to severe and peculiarly uncomfortable reactions in persons who have acquired a sensitivity to toxoid. Percutaneous immunization⁸² has been tried without success, and intradermal immunization⁸³⁻⁸⁶ has also been employed, with better results in some hands⁸⁶ than in others.⁸⁶ As might have been expected, reactions were more marked following intradermal administration of APT than when FT was used.^{85, 88}

Bousfield,⁸⁷ who⁸⁸ has explored various unusual routes of immunization against diphtheria, has recently suggested the use of toxoid pastilles to be sucked like hard candy. He reports that evidence for their effectiveness in primary immunization is lacking, but that they elicit an effective booster response and do not provoke local or general reactions. Finally, mention should be made of the protamine-toxoid combination developed by Ross,^{89, 90} which appears to be remarkably high in potency and which produces little reaction. Both preparations warrant further study.

Reimmunization The importance of reimmunization at some time subsequent to the primary immunization is apparent from the findings cited above. The dose required is often exceedingly small. Twenty years ago Glenn⁹¹ called attention to the booster effect frequently observed after a Schick test performed with material containing about one fifteen hundredth as much antigen as the corresponding volume of the average toxoid. Wishart et al.,⁷⁵ Volk et al.,⁹² Wilkey⁹³ and others have presented impressive evidence of the rapid and powerful effect of a booster dose of toxoid in persons with previously acquired immunity. The rises observed may be tremendous (over seven thousand times the minimum protective titer) and long lasting (three months or more).¹⁶ Nevertheless, adequate responses were not recorded in some subjects until about a week had elapsed,⁷⁵ so that the method is not completely dependable as an immediate protective measure following exposure to diphtheria. For the routine maintenance of group immunity, however, it has quite properly been widely advocated as a periodic health measure, particularly in localities where the natural incidence of diphtheria is too low to provide the necessary booster effect.⁹⁴

Immunization of infants It has long been taught⁹⁵ — and is doubtless generally true — that the best time for immunization of infants is after the first six months, because prior to this period the passively inherited maternal immunity interferes with the active effect of toxoid. Yet such a postponement leaves unprotected the currently increasing number

out. The wound may be so slight that medical aid is not sought or injury is not suspected. Antitoxin may not be readily available, the child may be allergic or may have received serum previously, and the ever-frequent serum sickness is always possible. Such considerations may influence the decision to take a chance and withhold serum.

The introduction of tetanus toxoid as an active immunizing agent offered a means of prevention that obviated many of these objections. The development and use of tetanus toxoid have been reviewed by Jordan and Halperin,¹⁴² Newhouse¹⁴³ and others. A great many investigators have clearly established the capacity of tetanus toxoid to produce significant and presumably protective serum antitoxin levels in human beings. So many individual variables — such as age of patient, kind of immunizing agent, size of dose, interval between doses and accuracy of titrations — have been introduced that evaluation of the data in such studies is extremely difficult. Furthermore, the problem of interpreting the reported results is illustrated by such passages as the following:

From the data it was deduced that when the initial tests were done within two months of giving the combined toxoids and the comparative tests showed the antitoxin values to be higher, the same or even lower after the respective third and second doses, then the tests performed from seven to twelve months later revealed not only that the drop of the titre was retarded after the third dose but that the antitoxin values were also higher.¹⁴⁴

It is possible, however, within certain limits, to define the principal results by means of the following considerations:

Number of doses required. One dose produces almost no detectable immunity but prepares the subject to react effectively to subsequent doses.¹⁴⁵ Acceptable results are obtained by the administration of three doses of FT (fluid toxoid) or two doses of APT (alum-precipitated toxoid). Ramon¹⁴⁶ has from the beginning recommended three doses of fluid toxoid, and the inadequacy of two doses of this agent has recently been confirmed.¹⁴⁷

Choice of interval between doses. For satisfactory results successive doses at least two weeks apart,¹⁴⁶ and preferably four weeks apart, are necessary. Peshkin,¹⁴⁸ Gold¹⁴⁹ and others have shown that excellent results are achieved even with intervals as long as two years between doses of APT. The limit to such extended intervals appears to be determined only by the period during which one can afford to wait before obtaining adequate immunity.

Choice of product. The principal advantages and disadvantages of each form of tetanus toxoid are essentially the same as those pointed out above for diphtheria toxoid. Dose for dose, APT is more effective than FT,¹⁵⁰⁻¹⁵² although the data in some cases are not properly comparable. The use of APT by the United States Navy and FT by the United States Army during the war should provide an un-

paralleled basis for comparison between the two, if the available data are ever analyzed.

Response to primary immunization. Practically all workers have observed marked variation in individual responses to primary immunization and have found occasional subjects in whom no detectable response appeared. In general, however, as with all immunization procedures for which accurate data are available, the antibody titer following primary immunization rises slowly to a maximum and then falls, at first rapidly and later more slowly, for as long as it can be detected. Obviously, the interpretation of results depends considerably on the interval chosen for the test. The actual interval between completion of immunization and development of a presumably protective antitoxin titer has been variously observed¹⁵³⁻¹⁵⁵, significant levels have been noted, however, as early as two weeks after immunization.

Protective level of antitoxin. Various workers have attempted — by analogy with titers observed following passive immunization¹⁵⁶⁻¹⁶¹ or by observing the titers in guinea pigs that were associated with protection against tetanus toxin¹⁵⁵⁻¹⁵⁶ or spores¹⁵⁷⁻¹⁶² — to estimate the level of antitoxin that will protect against clinical tetanus. These and other estimates range generally from 0.01^{148, 155-157} to 0.1 unit,¹⁴⁰⁻¹⁵⁹ but are of little practical value until they can be correlated with clinical experience, which has yet to be done.

Clinical evaluation. Massive clinical experience, although not correlated with serum antitoxin levels, has provided extensive statistical material for evaluating the efficacy of toxoid. Immunization of 40,000 horses in the French Army reduced the tetanus deaths in this group from the previous level of 50 to a single death.¹⁶³ In the retreat from Dunkirk, no cases of tetanus occurred among British soldiers protected with toxoid.¹⁶³ Among the more than 10,000,000 soldiers in the United States Army during World War II, there were only 3 known cases of tetanus in soldiers whose immunization record showed that the full immunization schedule had been completed.¹⁶⁴ The somewhat less perfect record in the British Army¹⁶⁵ may reasonably be ascribed to its policy of omitting the booster dose after injury and recommending antitoxin instead. Boyd¹⁶⁶ minimizes the value of the booster dose, arguing that it cannot be effective in less than ten days and that the infection itself serves as a booster after this interval in persons who have received primary immunization. It has been shown in animals,¹⁶¹⁻¹⁶² however, and in man,^{144-153, 154} that a marked response to toxoid appears by the fifth to seventh day. Moreover, this response is earlier and more effective in animals than the booster effect of infection itself.¹⁶¹⁻¹⁶² Boyd lists 22 cases of tetanus (with 11 deaths) among soldiers or others who had been protected with two or more doses of toxoid. Out of 15 soldiers in the British, Indian or Dominion

licated on the average a lasting immunity of about 60 or 70 per cent, although better results may be found in early follow-up Dick tests. Several years ago the Dicks¹¹⁹ reported that 93 per cent negative tests were obtained following the oral administration of over 8,000,000 STD in enteric-coated tablets. The wider development of this method has been hampered by the expense of preparing this quantity of toxin in powdered form and by the difficulty of ensuring its proper absorption. No recent reports on this interesting method have been noted.

Attempts have been made to reduce the reactions following scarlatinal toxin injection by purifying the crude toxin. Stock,¹²⁰ Veldee¹²¹ and others have employed various methods for separating the toxin from the other constituents of the medium, it is in fact possible to prepare toxins of extremely high purity by such means. In these preparations relatively few side reactions are caused by impurities, but their primary toxicity is unchanged. Hence, other means of preparing a tolerable product must be resorted to. Several workers have prepared toxin precipitated with alum¹²² or adsorbed on aluminum hydroxide.¹²³⁻¹²⁵ Menten et al.,¹²⁵ who for unexplained reasons refer to their product as a "toxoid," found that it yielded a higher Dick-negative rate than that observed in other groups immunized with a fluid toxin, and that it caused fewer reactions. The possibilities of this procedure call for further study.

Veldee et al.¹²⁶ have prepared a tannic-acid-precipitated, purified toxin that, modified slightly, was used in an extensive field study, comprising over 41,000 person-years of observation in an immunized group and a carefully analyzed and much larger control group. It was demonstrated that approximately 87 per cent of Dick-positive reactions in children before immunization became negative and remained so for four years after immunization with three intradermal injections of 750, 3000 and 10,000 STD of this toxin at intervals of two weeks. Similarly, the incidence of scarlet fever among the entire immunized group was only about one fifth that in the control group. Reactions were rare, and no child or parent refused to complete the entire course. The study was carried out with very thorough and accurate statistical and epidemiologic controls. The results appear highly promising, and it is hoped that, since a tannic-acid-precipitated toxin has been approved by the Council on Pharmacy and Chemistry of the American Medical Association,¹²⁷ further trials of this preparation will be forthcoming.

Attempts to produce a scarlet-fever toxoid have been carried out by numerous workers. Following the encouraging results obtained by Veldee,¹²⁸ a formalinized toxin was given extensive trial in Massachusetts. A preliminary report by Anderson¹²⁹ on the results with such a preparation, administered in doses of 0.1, 0.5 and 1.0 cc subcutaneously at intervals of three weeks, showed that approximately 52 per cent Dick reversals were obtained, and that

the number of cases of scarlatina in the immunized group was only about 60 per cent of that to be expected from analysis of the control group. Reactions to the product were few and mild, and only 11 per cent of 9200 children failed to complete the course of three injections. Results obtained with subsequent and more potent batches of toxoid have probably been better than Anderson's figures indicate.¹³⁰ Unless strikingly improved immunization can be produced with such a preparation, however, it will probably be abandoned in favor of one with a higher antigenic potency. Since the Scarlet Fever Committee patent expired four years ago and since the restrictions on the free development of scarlet-fever prophylactics other than the Dicks' immunizing toxin have accordingly been removed, it can be expected that active and productive research in this heretofore relatively static field will proceed vigorously to the development of a satisfactory prophylactic agent.

TETANUS

Tetanus has always been a serious menace to war casualties, but even under the conditions of Western civilization in peacetime the possibility of its occurrence must constantly be borne in mind. Adequate cleaning and débridement of wounds remains the first defense against tetanus. Treatment of wounds can never be relied on to prevent all cases, however, for as many as 50 per cent may not be traceable to a known injury^{131, 132} and many other cases follow neglect of such minor infections as those produced by a splinter. Since the tetanus bacillus is found even in city streets,¹³³ the possibility of infection with this organism is ever present.

Until recent years protection against tetanus was obtained largely through the prophylactic use of tetanus antitoxin. MacConkey¹³⁴ reviewed the experience with this agent in World War I and called attention to the occasional failures to obtain protection. Failures are also recognized in civilian experience, of the 146 tetanus cases reported by Dietrich,¹³¹ Klopp¹³⁵ and Kirtley,¹³⁶ 11 patients had received prophylactic antitoxin, and 8 of the 11 died. Among a group of 15,000 to 20,000 casualties of the blitz of 1940 in England, 7 definite cases of tetanus occurred, in all but 1 of which 1000 to 1500 American units of antitoxin had been administered shortly after injury.¹³⁷ In the retreat from Dunkirk, 8 cases occurred in wounded soldiers who had never received toxoid and who had to rely on antitoxin prophylaxis.¹³⁸ Such irregularities appear to result mostly from the varied rate at which the antitoxin is eliminated from the blood stream.^{44 139-141} Thus the results obtained with prophylactic antitoxin are undependable, the more so because tetanus infection may exhibit a prolonged time lag between its introduction and its activation. Moreover, the disadvantages of antitoxin for prophylaxis are not limited to its undependability, as Bigler and Werner⁴⁴ have pointed

The best type of schedule might well be adapted from that of the United States Army³⁵ primary immunization with two doses of APT or three of FT at intervals of one month or longer, followed by at least one recall dose six to twelve months later and another recall dose after any injury of the sort that is known to involve the risk of tetanus infection. The available evidence suggests that active immunity is acquired within two weeks after the primary immunization is completed, but it is nevertheless wise to heed the warning of Tuft⁴² and carry out immunization so far as practicable in advance of possible exposure to tetanus. The practice of administering prophylactic antitoxin routinely following accidents or injuries will have to be greatly modified in civilian practice. When such injuries occur to persons who are known to have been actively immunized, such as all veterans of World War II, emergency prophylaxis should be obtained by administering a booster dose of toxoid.¹⁹²

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forces, 10 had received three or more doses. Only 4 men had been given four, and 2 had been given five doses. Since the standard procedure in the United States Army calls for at least four and usually five doses of toxoid as well as the emergency booster dose at the time of injury, the cases of tetanus reported here and elsewhere¹⁶⁶⁻¹⁶⁸ in British and Colonial troops do not, as has been suggested,^{169, 170} provide a valid criterion of the efficacy of tetanus toxoid prophylaxis performed according to current American practice.

The booster dose. On receiving a booster dose of toxoid, a previously immunized person exhibits a marked and rapid rise in serum antitoxin titer.^{142, 144, 146, 150, 152, 171-173} Hence it has been generally advocated in this country that recall doses be given periodically, to restore the immunity level, which gradually falls after primary or later stimuli, and after injury to produce a maximal antitoxin level at the time of the greatest danger of toxin absorption. Some writers have assumed that the absorption of tetanus toxin in itself provides a sufficient booster effect,¹⁵⁰ but the available evidence indicates that tetanus infection does not act as a primary stimulus to antitoxin production^{152, 159} and gives a secondary stimulus too late to be dependable.^{161, 162} Therefore, until it is possible to define what constitutes a protective serum antitoxin level and to perform a simple test for the presence of this degree of protection, the only way to assure the maximum degree of protection is to make the most of the booster dose, by giving supplementary injections of toxoid following known injuries and by giving periodic doses to ward off the tetanus infections that can occur after unnoticed injuries. The efficacy of the booster dose does not appear to decrease as the interval between it and the primary immunization increases. Peshkin has obtained excellent booster responses one,¹⁴⁴ two,¹⁷⁴ three¹⁷⁵ and four¹⁷⁶ years after primary immunization. Furthermore, with each subsequent recall dose, the antitoxin titer usually rises higher and remains elevated longer.^{176, 177} Yeazell and Deamer¹⁴¹ employed intradermal toxoid successfully for the booster dose. It has been shown in animals that the booster response is but little affected by cold, restricted diet or overwhelming infection.¹⁷⁸ The only limiting factor in utilizing the booster effect appears to be the time interval between injection and response. The occasional subject whose response is slow might conceivably cause some anxiety, but clinical experience, as in the United States Army, strongly indicates that the rate of response to a booster dose is adequate. Finally, since the titer achieved following a booster dose remains elevated for several months,^{144, 154, 174-176} frequent repetition of doses, such as those that must be relied on in prolonged antitoxin prophylaxis, is not necessary.

Other routes than the subcutaneous for administration of tetanus toxoid have been employed rela-

tively little. Gold¹⁷⁹ and Sordelli et al.¹⁸⁰ gave booster doses intranasally, with apparently satisfactory results. Friedman and his associates¹⁸¹ employed intradermal inoculations, but the results were decidedly less satisfactory than those obtained by the usual subcutaneous route.

Active-passive immunization. No clear-cut answer has yet been given to the dispute regarding combined active and passive immunization. In a patient exposed to tetanus, never previously immunized and requiring prophylactic antitoxin, one school of thought maintains that simultaneous commencement of active immunization with toxoid is ineffective because of the presence of excess antitoxin.¹⁸¹ Another school has for over twenty years maintained that simultaneous active-passive immunization can be successfully practiced.^{182, 183} The official policy of the United States Army has been to administer antitoxin prophylaxis only if an initial course of active immunization has not been completed and to start simultaneous active immunization.³⁵

Allergic reactions. Such reactions, which have been reported to both FT and APT,^{35, 151} have been amply reviewed by Long,³⁵ who showed that the urticarial type resulted from the presence of Witte or Bernal peptone in the toxoid medium. The elimination of these ingredients from subsequent preparations has apparently virtually eliminated this type of untoward reaction. One of Swartz's¹⁸⁴ cases, however, may have represented a sensitivity to some ingredient in the toxoid other than peptone. The studies of Mueller¹⁸⁵ and of Taylor¹⁸⁶ on the production of toxin on simplified media and the recently reported successful purification of tetanus toxin¹⁸⁷ should lead to the preparation of toxoids possessing but a minimal capacity to induce sensitization phenomena. Meanwhile, many reports of successful and virtually reaction-free tetanus toxoid immunizations, including large numbers of allergic subjects,^{140, 141, 144, 148, 154, 174-176, 180, 188, 189} suggest that the danger of allergic reactions in atopic subjects is no greater than that in normal persons—in marked contrast to the danger of using antitoxin in such subjects.

Indications for immunization. The indications for the employment of tetanus toxoid have been well summarized,¹⁹⁰ as follows: in allergic persons or those with known sensitivity to horse serum, in farmers, hostlers, veterinarians, horsemen and others experiencing relatively frequent opportunity for contamination of wounds with tetanus spores, and by and large in children, among whom the incidence of infected wounds is high and many unnoticed infections may result in tetanus. The combination of tetanus toxoid with diphtheria toxoid for immunization of children therefore appears wise not only in private practice but also as an adjunct to diphtheria-control programs.

The best type of schedule might well be adapted from that of the United States Army³⁵ primary immunization with two doses of APT or three of FT at intervals of one month or longer, followed by at least one recall dose six to twelve months later and another recall dose after any injury of the sort that is known to involve the risk of tetanus infection. The available evidence suggests that active immunity is acquired within two weeks after the primary immunization is completed, but it is nevertheless wise to heed the warning of Tuft¹¹ and carry out immunization so far as practicable in advance of possible exposure to tetanus. The practice of administering prophylactic antitoxin routinely following accidents or injuries will have to be greatly modified in civilian practice. When such injuries occur to persons who are known to have been actively immunized, such as all veterans of World War II, emergency prophylaxis should be obtained by administering a booster dose of toxoid.¹⁹²

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIFTH ANNIVERSARY

House of Delegates, May 13 and 14, 1946

THE House of Delegates convened at the Hotel Carpenter, Manchester, on May 13, 1946, at 7 30 p m., with Speaker Deering G. Smith presiding. The following members answered the roll call:

The President, *ex-officio*
 The Vice-President, *ex-officio*
 The Secretary-Treasurer, *ex-officio*
 Samuel Feiner, Ashland
 Earl J. Gage, Laconia
 Francis J. C. Dube, Center Ossipee
 W. J. Paul Dye, Wolfeboro
 Albert C. Johnston, Keene
 James M. Ballou, Keene
 Marjorie B. Parsons, Colebrook
 Francis M. Appleton, Gorham
 Howard N. Kingsford, Hanover
 Israel A. Dinerman, Canaan
 Leslie K. Scamore, Hanover
 Robert E. Biron, Manchester
 George C. Wilkins, Manchester (alternate for Samuel Fraser)
 Loren F. Richards, Nashua
 Robert R. Rix, Manchester
 Deering G. Smith, Nashua
 Frank J. McQuade, Franklin
 William P. Clough, Jr., New London
 Philip M. L. Forsberg, Concord
 Willard C. Montgomery, Epping

Samuel T. Ladd, Portsmouth
 Robert W. Tower, Plaistow
 William R. Latchaw, Somersworth
 Raymond R. Perreault, Rochester
 Addison Roe, Newport
 B. Read Lewin, Claremont

The Speaker declared a quorum present, and appointed the Credentials Committee as follows: Drs. Appleton, Latchaw and Feiner. To the Committee on Officers' Reports, he appointed Drs. Lewin (chairman), Biron and Montgomery. To the Committee on Communications and Memorials he appointed Drs. Dinerman, Tower and Perreault. To the Committee on Nominations, he appointed Drs. Richards (chairman), Gage, Forsberg, Dye and Ladd. For the Committee on Credentials, Dr. Appleton reported that the credentials were in order.

On motion duly made and seconded, it was voted to omit the reading of the previous minutes, because of the publication of the proceedings.

On motion duly made and seconded, it was voted to dispense with the reading of the reports of the councilors, since they will be published in the *Transactions*.

The Secretary-Treasurer, Dr. Carleton R. Metcalf, presented his report, as follows:

MEMBERSHIP, DECEMBER 31, 1945

PAID	
Belknap County	23
Carroll County	9
Cheshire County	17
Coos County	21
Grafton County	58
Hillsborough County	98
Merrimack County	53
Rockingham County	46
Strafford County	29
Sullivan County	14
Not in County Society	3
	371
UNPAID	
Life members	18
Honorary members	5
Members in service and delinquents	134
	157
	528

The total membership on December 31, 1944, was 546

FINANCIAL STATEMENT

RECEIPTS

January 1 1945 — balance forward	\$677 42
Belknap County	156 00
Carroll County	66 00
Cheshire County	78 00
Coos County	156 00
Grafton County	342 00
Hillsborough County	588 00
Merrimack County	348 00
Rockingham County	282 00
Strafford County	174 00
Sullivan County	84 00
Cash received at annual meeting	119 00
Members not in county societies	18 00
Refund (Cancer Committee)	18 80
Donations to National Physicians Committee	93 00
(Merrimack County, \$50, Strafford County, \$29, Sullivan County, \$14)	
Benevolence Fund (Hillsborough County)	40 00
	\$3240 22

EXPENDITURES

<i>New England Journal of Medicine</i>	
Journals	\$483 93
Transactions	1168 46
Tables	4 23
Carleton R Metcalf (salary)	500 00
Printing	104 00
Envelopes and stamps	47 17
Halftone cuts	28 90
Clerical work	111 50
Telephone and telegraph calls	19 77
Retaining fee	100 00
Guest speakers (fees)	26 93
Cancer Committee	40 00
Cash collected at annual meeting	77 00
Benevolent Fund	
Hillsborough County	40 00
Merrimack County (received in 1944)	20 00
National Physicians Committee (donations)	
Merrimack County	50 00
Strafford County	29 00
Sullivan County	14 00
Strafford County (received in 1944)	28 00
Madeline A May (stenographer at annual meeting)	226 87
Flowers (H O Smith)	12 38
Service charges at bank	84
	\$3132 98
Balance, January 1, 1946	107 24
	\$3240 22

The total membership on December 31, 1945, was 528. This is a decrease of eighteen over the preceding year.

The following officers died during the year 1945: Clifton S. Abbott, Laconia; Henry O. Smith, Hudson; Herbert L. Taylor, Portsmouth; and Richard E. Wilder, Whitefield.

Although no money was added to the Benevolence Fund from the annual dues during 1945, a donation was received from the Hillsborough County Auxiliary. Ninety-three dollars for the National Physicians Committee was received from the following auxiliaries: Merrimack County, Strafford County and Sullivan County.

In accordance with instructions from the House of Delegates, \$40.00 was given to the Cancer Committee. The question of outpatient psychiatric care in New Hampshire was referred to the Committee on Mental Hygiene, with the request that it consider the matter and report at this meeting.

A report on the New Hampshire Physicians' Service, or Blue Shield, which was inaugurated and sponsored by the House of Delegates, will be given by its president, Leslie K. Sycamore.

I recommend that we drop the following two standing committees this year: the Committee on O. P. A. Assistance and the Committee on Medical Preparedness. On the other hand, we should add one new standing committee because during the last year the Council of the State Medical Societies of New England has been rejuvenated. This council held three or four meetings and considered medical matters that pertained to all the New England states, particularly matters of national legislation. Dr. Robinson, Dr. Sycamore and I attended two meetings as unofficial delegates from New Hampshire and we gave the Council \$100.00 from the treasury of this society to help pay the running expenses. I suggest that the House of Delegates approve this fee and apportion \$100.00 each year for the same purpose and that the Committee on Nominations recommend a standing committee of three for membership on this council. Now that many of the members of this society have returned from the Armed Services, I also suggest to the Committee on Nominations that our various committees be strengthened by the appointment of a due proportion of younger men and of veterans. The Committee on Nominations should also note that Dr. Fitch has resigned as alternate delegate to the American Medical Association.

The annual meeting this year is limited to one day for two reasons: it is difficult to get hotel accommodations to stay overnight in Manchester, and a one-day meeting is less expensive than a longer meeting and we have been "in the red" for the last few years. I hope, however, that next year and thereafter we may return to our former plan of having the annual meeting last for two days. Some members of the Society have suggested that the meeting next year be held during June at one of the resort hotels, for example, a hotel at Portsmouth or one at Sunapee. A scheme of this sort has been followed for many years by the Maine Medical Association, whose members seem to like it. I recommend that the House of Delegates give it consideration.

In view of our somewhat embarrassed financial position, I recommend an increase in the annual dues of the Society. The present by-law reads "an assessment of \$6.00 per capita on the membership of the component societies is hereby made the annual dues of this society." If this assessment were increased to \$9.00, we should be able to carry on much better in an era in which expenses have slowly but surely become greater. Such an increase would presumably mean that each member of the county society would pay \$10.00, of which \$1.00 would be retained in the county and \$9.00 turned over to this organization. I have referred this matter to the Committee on Amendments. If it meets with the approval of this committee and your approval, the amendments should first be made in the House of Delegates and then ratified by each county society.

It is of interest to note that the Vermont State Medical Society has recently raised its annual dues to \$20.00, so that the increase that I have suggested seems relatively modest.

At the present time, the *New England Journal of Medicine* has been sent to each of our members once a month. Recently the *Journal* has suggested a modification of the arrangements as follows:

Either one of two arrangements is possible. The first is to send all issues of the *Journal* to the members of your society at a charge of \$2 50 for the current year. This, of course, would probably mean an increase in the annual dues of \$1 50. On the other hand, it seems likely that your members would derive a reasonable amount of benefit. The second is to continue with the present arrangement so far as all members of your society are concerned, but to permit any member to subscribe individually for all issues at an extra cost of \$1 50.

So far as the future is concerned, the rate of \$2 50 cannot be guaranteed. It seems reasonably certain, however, that there will not be an appreciable increase in cost, and if the circulation continues to increase and the advertising revenue is maintained, it might well be lowered.

At the present time the Society pays the *New England Journal of Medicine* \$1 00 a year for each member.

I should recommend the second alternative continue the present arrangement, but permit any member who wishes all issues to procure them by sending a check of \$1 50 directly to the *Journal*.

At the time this report is being written, the Wagner-Murray-Dingell Bill is being considered by the Committee on Education and Labor of the United States Senate. In accordance with the instructions passed by the House of Delegates, the Committee on Public Relations has been active in opposing this legislation.

Dr Robinson and I spent two days last February at a meeting of the National Physicians' Committee in St. Louis, where this and other federal legislation was thoroughly discussed. Here in New Hampshire, through the press and through personal contacts with various groups, we have tried to present the point of view of the Society, and many of these groups have co-operated with us in expressing their disapproval to our Congressional delegation. The end result is that as this report is written Senator Bridges, Congressman Adams and Congressman Merrow have stated that they would vote against the present Wagner Bill. Senator Tobey has been noncommittal.

On motion duly made and seconded, it was voted that the report of the Secretary-Treasurer be referred to the Committee on Officers' Reports.

Dr Lewin, chairman of the Committee on Officers' Reports, then stated that the Committee on Officers' Reports had recommended that the Nominating Committee create a new standing committee of three members, to be called the Committee of New England Medical Societies. He moved the adoption of this portion of the report. The motion was duly seconded.

The President expressed some doubt whether a new committee could be created by the Nominating Committee, since this was a matter of the by-laws of the Society and would require an amendment.

Dr Dye stated that the various standing committees came under the by-laws and the constitution, and that such a motion could therefore be recommended one day, put on the table that night and voted on the following day. He recommended such an amendment.

The Speaker requested the Secretary's opinion.

The Secretary replied that it was much easier to have all the committees on the same basis, and that they could be changed when necessary.

The President stated that he saw no reason why a special committee could not be appointed.

The Speaker asked for the motion again.

Dr Lewin moved that the House of Delegates instruct the Nominating Committee to create a new

standing committee of three members, to be called the Committee of New England Medical Societies.

Dr Dye moved that Chapter VIII of the by-laws be amended to include the committee recommended by the Committee on Officers' Reports. This motion was duly seconded.

Dr Lewin moved that the House of Delegates approve the \$100 00 given to the Council of the State Medical Societies of New England during this last year. This motion was duly seconded and carried.

Dr Lewin then moved that \$100 00 be appropriated for the Council of the State Medical Societies of New England this year.

This motion was duly seconded and carried.

Dr Lewin stated that the Committee on Officers' Reports had reached no conclusion regarding the site of future meetings. He recommended open discussion by the delegates.

Dr Sycamore stated that the delegates from Grafton were instructed to change the meeting place next year and asked whether such a decision were the province of the Program Committee.

The Speaker replied that the matter was one for decision by the House of Delegates.

Dr Sycamore moved that the House of Delegates be empowered at least to investigate another site for a meeting for next year and to adopt another site if a suitable one were available.

The Secretary observed that the situation has been complicated by transportation and by hotel accommodations, with practically no rooms available in Manchester. If a two-day meeting were held, the members who lived at a distance would probably have to come for only one day. The thought in suggesting this matter was that the Society could meet in some place like the Wentworth in Portsmouth. He further stated that the Wentworth advertises for conventions, which they can accommodate any time after June 1. He added that the housing problem would be solved at the Wentworth.

The Speaker asked if there was any further discussion on this subject.

Dr Ladd believed that the Wentworth would be a desirable place for the meeting.

The Speaker called attention to the fact that the by-laws state that the Society shall hold an annual session, during which there shall be held daily not less than two general meetings open to all registered members, delegates and guests, and that the place for holding such annual session shall be fixed by the House of Delegates, and the date by the President and the Secretary-Treasurer.

Dr Wilkins moved that the next meeting be held in Portsmouth at the Wentworth.

The motion was duly seconded by Dr Dye.

The Secretary suggested that power be given to someone to select a place, so that if the Wentworth burned down a special meeting would not have to be called.

Dr Wilkins accepted the amendment.

The Speaker asked for the opinion of those who wanted a two-day meeting. There was a unanimous showing of hands. He then stated that the motion before the House was that the next meeting of the Society should be held at the Hotel Wentworth in Portsmouth, and that if that site were not available, the President, together with the Vice-President and the Secretary, would select the site. The motion was carried.

Dr Lewin, for the Committee on Officers' Reports, moved that the present arrangement, namely, that the Society pay the *New England Journal of Medicine* \$1 00 a year for each member be continued, but that any member who wished all issues of the *Journal* obtain them by sending a check for \$1 50 directly to the *Journal*.

This motion was duly seconded, and was carried.

Dr Lewin, for the Committee on Officers' Reports, then moved that Dr Metcalf's report be accepted in full.

This motion was duly seconded and was carried.

Dr Paul Dye for the Committee on Amendments to the Constitution and By-Laws, made the following recommendations to amend Article IV, Section 1, of the constitution, to read as follows: "This society shall consist of members, life members and honorary members", to amend Section III, Article 4, to read as follows: "life members shall be those members whose dues are remitted".

Dr Dye stated that these changes had been accepted unanimously by the House of Delegates in 1945 and presented in open meeting at the annual session, and should therefore come up for a final vote at the 1946 meeting.

Dr Dye also recommended that Section 1 of Chapter 10 of the by-laws be amended to read as follows: "An assessment of \$9 00 per capita on the membership of the component societies is hereby made the annual dues of this society." He pointed out that this provision meant that each county society should charge \$10 00 for its membership, retaining \$1 00 for itself and sending \$9 00 per member to the New Hampshire Medical Society, presumably, each county society would have to take similar action under its by-laws to cover these increased dues.

The Speaker stated that although this matter was presumably to be laid on the table for discussion until the following morning and although no formal action could be taken immediately, it might be wise to discuss it.

A member inquired if \$3 00 were a sufficient increase.

The Secretary stated that this increase would raise the dues enough for the coming year, and recommended such an increase, which could be raised further if great expenses were incurred.

Dr Biron recommended raising the dues to \$10 00, which would pay an assessment in toto of \$11 00.

The Speaker stated that Hillsborough County had added an assessment of \$1 00 to the dues this year,

and that every man except one had paid the \$8 00 rather than \$7 00.

The Secretary pointed out that any excess, no matter what the dues were, was turned back to the Trustees. Up to the beginning of the war, something was returned every year for the General Fund, since the beginning of war, money had been borrowed from the Trustees at the rate of \$500 to \$1000 a year.

Dr Wilkins proposed that the dues be increased to a figure that would be sufficient to support the activities of the Society, believing that if the dues were \$12 00, or anything above \$10 00, such an amount would be better than \$9 00.

The Speaker requested that all those in favor of raising the dues raise their right hands.

The decision to increase the dues was unanimous.

The Speaker then asked how many wanted the dues raised to \$9 00 or \$10 00.

Dr Montgomery inquired if there were any objection to raising the dues to \$14 00, making the total \$15 00.

The Speaker asked how much money had been withdrawn from the General Fund.

Dr Wilkins replied that \$500 had been withdrawn and that he believed that more than \$500 had been withdrawn during the previous year.

It was asked how much money was in the General Fund.

Dr Wilkins replied that there was \$4957 74 in the General Fund — a much smaller amount than had been in the Fund a few years previously because during the war the general reserve funds that had been established had been depleted to help the general running expenses of the Society.

The Speaker stated that the reserve fund could be drawn on, if necessary, whereas the other funds, like the Benevolence Fund, could not be touched.

The Secretary said that nothing had been given to the Benevolence Fund for the last three or four years.

The Speaker asked that all those in favor of \$14 00 a year raise their hands. Sixteen hands were raised. He then requested those opposed to \$14 00 per year to raise their hands. Seven hands were raised.

Dr Clough stated that on the basis of 528 members in the Society, \$2500 would be put into the General Fund, approximately \$1500 had been withdrawn in the war years, and \$2500 would be replaced. He asked for an explanation why that amount was needed in the General Fund.

Dr Lewin, as secretary of the Sullivan County Medical Society, expected to encounter some difficulty in collecting \$15 00, and believed that many of the members would greatly object.

Dr Sycamore stated that many members of the Society discharged from the armed forces might have some difficulty in meeting various extra expenses that returning to civilian life entails. He suggested that the dues might be raised sufficiently

to cover expenses for the year and that the following next year, if necessary, the dues be increased again

Dr Ladd invited attention to the fact that the \$15 00 could be deducted from income taxes, and stated that in his county the reserve fund had mounted to around \$400 or \$500

A question was asked if the General Fund were a fund to be drawn on during the war years and if there were any other functions of the fund

The Speaker replied that the Secretary had informed him that there was no other function of the General Fund, except as a reserve fund

Dr Wilkins stated that it was the General Fund that has been built up. Analysis for seven or eight years had revealed that the New Hampshire Medical Society was not self-supporting: the money received and the money paid out for various expenses required \$500 a year more from the general fund. The dues collected did not carry or cover the cost of the running of the Society, and in a year in which no money was received from the exhibitors there had been a large deficit, a similar deficit had occurred in the previous two or three years, with only a one-day meeting and with a decrease in the amount received from the exhibitors. To meet expenses, the dues of the society must be raised at least \$1 00

Dr Biron inquired whether, when the Secretary made his estimate, he considered that such a sum would not only carry the annual meeting for the next year but also perhaps repay some of the loan received from the General Fund. If so, Dr Biron believed that the estimate should be considered sufficient

The Secretary replied that he did not know exactly how much, if anything, could be paid back, but that the Society could get by on a rate of \$10 00

Dr Wilkins pointed out that the Society had always been in the position of being partially supported by the exhibitors. He believed that the Society should be able to support itself

Dr Montgomery remarked that a two-day meeting would cost more than \$1 00, and more than the \$5 00 or \$6 00 that was being asked as an increase

Dr Ladd stated that speakers from outside the State cost \$100 00 each and that expenses were high

The President expressed his opinion that the dues should be increased sufficiently to meet the expenses of the Society, but saw absolutely no reason for making the dues any higher than necessary. Until the war, the Society had always had a two-day meeting, and the reports of the Treasurer for a number of years in normal times, even on the former rate, showed that there was enough money to add a little to the General Fund, which had no specific purpose and therefore no object for being built up. The money had not been loaned with the idea that it has to be paid back. This was an emergency fund. Consequently, the President was in favor of a reasonable amount such as \$12 00, but not \$14 00, and

preferably \$10 00. The Vermont State Medical Society was said to have raised its dues to \$20 00, but that increase was necessary because a full-time executive secretary was employed

The President observed that at meetings of the House of Delegates, year after year, delegates gave a good deal of their time and consideration to particular problems that were presented to the Society. In the following year, the minutes of the previous meetings of the House of Delegates, as is customary, were always left unread. The *Transactions* of the Society were printed in the *New England Journal of Medicine*, some in one issue and some in following issues, and as a rule were not read by most members. He believed that if the minutes of the meetings could be read, much of the discussion would be unnecessary. He added that some committee of the Society could profitably make a search through the minutes of the House of Delegates for the last six years, because the time saved and duplication avoided would tend to give a progressive structure to the deliberations of the House of Delegates

The Speaker stated that the minutes of the previous meeting occupied about forty-five pages of the *Transactions* and would take about two hours to be read

The President said that if a member or a committee could bring to the House of Delegates a summary of the actions taken, and a report of whether the will of the Society had been carried out, the whole procedure would be much improved

Dr Dyé stated that a small addition to the Secretary's estimate of \$9 00 would probably ensure sufficient funds for the operation of the Society. He therefore moved that the annual dues of the Society be raised to \$10 00

This motion was duly seconded by Dr Dinerman, and on a showing of hands, the opinion was unanimous, although no official vote was taken

Dr Dye then announced that he would submit the vote for the amendment at the meeting on the following morning

Dr Lewin, in the absence of the chairman, read the report of the Committee on Child Health, as follows

The Committee on Child Health has been relatively inactive. A most important step toward the betterment of the health of the children of New Hampshire is the study of child-health services of the American Academy of Pediatrics, which is now in progress. We urge the co-operation of all the members of the Society in this study

COLIN C STEWART, *Chairman*
B READ LEWIN
FRANKLIN ROGERS

Dr Lewin moved that this report of the Committee on Child Health be accepted

This motion was duly seconded

The President stated that a physician from Massachusetts engaged in work of a similar nature to that reported would present a résumé on the child-

The Speaker asked for the opinion of those who wanted a two-day meeting. There was a unanimous showing of hands. He then stated that the motion before the House was that the next meeting of the Society should be held at the Hotel Wentworth in Portsmouth, and that if that site were not available, the President, together with the Vice-President and the Secretary, would select the site. The motion was carried.

Dr. Lewin, for the Committee on Officers' Reports, moved that the present arrangement, namely, that the Society pay the *New England Journal of Medicine* \$1.00 a year for each member be continued, but that any member who wished all issues of the *Journal* obtain them by sending a check for \$1.50 directly to the *Journal*.

This motion was duly seconded, and was carried.

Dr. Lewin, for the Committee on Officers' Reports, then moved that Dr. Metcalf's report be accepted in full.

This motion was duly seconded and was carried.

Dr. Paul Dye for the Committee on Amendments to the Constitution and By-Laws, made the following recommendations to amend Article IV, Section 1, of the constitution, to read as follows: "This society shall consist of members, life members and honorary members", to amend Section III, Article 4, to read as follows: "life members shall be those members whose dues are remitted."

Dr. Dye stated that these changes had been accepted unanimously by the House of Delegates in 1945 and presented in open meeting at the annual session, and should therefore come up for a final vote at the 1946 meeting.

Dr. Dye also recommended that Section 1 of Chapter 10 of the by-laws be amended to read as follows: "An assessment of \$9.00 per capita on the membership of the component societies is hereby made the annual dues of this society." He pointed out that this provision meant that each county society should charge \$10.00 for its membership, retaining \$1.00 for itself and sending \$9.00 per member to the New Hampshire Medical Society, presumably, each county society would have to take similar action under its by-laws to cover these increased dues.

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A member inquired if \$3.00 were a sufficient increase.

The Secretary stated that this increase would raise the dues enough for the coming year, and recommended such an increase, which could be raised further if great expenses were incurred.

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and that every man except one had paid the \$8.00 rather than \$7.00.

The Secretary pointed out that any excess, no matter what the dues were, was turned back to the Trustees. Up to the beginning of the war, something was returned every year for the General Fund, since the beginning of war, money had been borrowed from the Trustees at the rate of \$500 to \$1000 a year.

Dr. Wilkins proposed that the dues be increased to a figure that would be sufficient to support the activities of the Society, believing that if the dues were \$12.00, or anything above \$10.00, such an amount would be better than \$9.00.

The Speaker requested that all those in favor of raising the dues raise their right hands.

The decision to increase the dues was unanimous.

The Speaker then asked how many wanted the dues raised to \$9.00 or \$10.00.

Dr. Montgomery inquired if there were any objection to raising the dues to \$14.00, making the total \$15.00.

The Speaker asked how much money had been withdrawn from the General Fund.

Dr. Wilkins replied that \$500 had been withdrawn and that he believed that more than \$500 had been withdrawn during the previous year.

It was asked how much money was in the General Fund.

Dr. Wilkins replied that there was \$4957.74 in the General Fund — a much smaller amount than had been in the Fund a few years previously because during the war the general reserve funds that had been established had been depleted to help the general running expenses of the Society.

The Speaker stated that the reserve fund could be drawn on, if necessary, whereas the other funds, like the Benevolence Fund, could not be touched.

The Secretary said that nothing had been given to the Benevolence Fund for the last three or four years.

The Speaker asked that all those in favor of \$14.00 a year raise their hands. Sixteen hands were raised. He then requested those opposed to \$14.00 per year to raise their hands. Seven hands were raised.

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Dr. Lewin, as secretary of the Sullivan County Medical Society, expected to encounter some difficulty in collecting \$15.00, and believed that many of the members would greatly object.

Dr. Sycamore stated that many members of the Society discharged from the armed forces might have some difficulty in meeting various extra expenses that returning to civilian life entails. He suggested that the dues might be raised sufficiently

ternal deaths was 16, with a slight decrease in the birth rate as compared with the previous year. There were 8551 births in 1945.

In the tabulations to follow, it is interesting that although most cases are classified as unavoidable, a greater number of cases were regarded as having received inadequate treatment than in previous years. Of the 16 deaths, the method of delivery reported for 8 of the cases was operative or "forced." The committee cannot stress too often the opinion that there is never any justification for an *accouchement force*.

In the twelve years during which this study has been conducted, the high point was reached in 1935, with a rate of 6.1 per 1000 live births, with 46 deaths. At this point it was easy to speculate that improved obstetrics, increased knowledge, better facilities of both hospitals and physicians and intensified programs for fostering better maternity care were responsible for a lower trend, and such factors may well have been responsible. The maternal death rate rose sharply in 1943, however, and continued to climb in 1944. These being war years, the scarcity of personnel, stresses of wartime and fewer facilities, especially in hospitals, may well have been to blame. Now that 1945 has written its page in history, it is truly encouraging to note the decrease in the maternal death rate.

The committee did not attempt to do an intensive study on infant deaths under one year, or of stillbirths, time and personnel were not available for such a study. Tabulations regarding causes of infant deaths, however, follow. Again the committee includes in this report the definition of a stillbirth that has become accepted in most states. There will always be some confusion in the reporting of stillbirths because of individual interpretations, especially since the period of gestation that must be reached before registration as a stillbirth, differs in many states.

MATERNAL DEATHS

In 1945, the period of this study, there were 16 maternal deaths. The number of live births was 8551. This gives a rate of 1.9 per 1000 live births. Since 1941, the birth rate has steadily climbed, probably because of an influx of population into defense areas and more marriages among servicemen. All deaths reported occurred in hospitals.

The following is a tabulation of maternal deaths by cause for the year 1945 as established by the committee and subdivided according to causes of death as assigned by the Division of Vital Statistics in accordance with the *International List of Causes of Death* (fifth edition).

CHIEF CAUSE ACCORDING TO INTERNATIONAL CODE	NO OF CASES
Other accidents of pregnancy and specified conditions of childbirth (including death before delivery)	6
Hemorrhage of pregnancy (including death before delivery and those of puerperium)	3
Infection during childbirth and puerperium	3
Abortions	2
Puerperal toxemia	2
Total	16
CHIEF CAUSE AS CLASSIFIED BY COMMITTEE	NO OF CASES
Puerperal emboli	4
Ruptured uterus	3
Toxemias (all types)	3
Myocardial failure	2
Nonmaternal	1
Hemorrhage of childbirth	1
Unknown (incomplete data)	2
Total	16

CAUSE OF DEATH	NO OF DEATHS AS ASSIGNED BY INTERNATIONAL CODE	NO OF DEATHS AS GROUPED BY COMMITTEE
Puerperal emboli		4
Abortion	1	
Other diseases and accidents of pregnancy (death before delivery)	1	
Infection during childbirth and puerperium	2	
Ruptured uterus		3
Other accidents and specified conditions of childbirth	1	
Hemorrhage of pregnancy (death before delivery)	1	
Hemorrhage of childbirth and puerperium	1	
Myocardial failure		2
Other accidents and specified conditions of childbirth	1	
Other diseases and accidents of pregnancy (death before delivery)	1	
Toxemias (all types)		3
Puerperal toxemia	2	
Infection during childbirth and puerperium	1	
Hemorrhage of childbirth and puerperium	1	1
Incomplete		2
Other accidents and specified conditions of childbirth	2	
Nonmaternal deaths		1
Abortion	1	
Total	16	16

In the 16 fatal cases 5 cesarean sections were performed. The causes of death recorded were as follows: toxemia 2, post-partum hemorrhage 1, ruptured uterus 1, and unknown 1.

In 3 other cases a forced delivery was performed, and the committee interprets such procedures as referring to an *accouchement force*. These reports reveal that almost half the deaths studied (8 cases) involved operative or forceful means of delivery, only 2 of which, in the opinion of the committee, were indicated because of either a previous section or an apparent disproportion. The committee cannot justify any cause for a forced delivery.

One case to illustrate a forced delivery occurred when the attending physician during the course of a normal labor in a twenty-three-year-old multipara observed that the fetal heart was accelerated. He became alarmed and called in a consultant. From the data obtainable on the report, it appeared that, with the cervix dilated but one fingerbreadth, the consultant performed what was recorded as a forced delivery, obtaining a stillborn child. The placenta showed some infarcts. The fact that some blood clots were observed led to a diagnosis of abruptio placenta, which was given as a cause of death. The patient went into shock following delivery and expired. The committee believes the diagnosis to be incorrect from the data, but believes that the patient died as a result of the treatment, presumably from a ruptured uterus resulting from the forced delivery. It is to be remembered that this conclusion was reached from the material at hand. Whether the membranes had ruptured previously was not known and it was not recorded whether the patient was examined after death for ruptured uterus.

It has been the usual procedure for the committee to classify these deaths further to illustrate if possible where the responsibility for maternal deaths belongs. The groups are as follows: Group 1, 2 cases in which the patient was at fault because of refusal of prenatal care, neglect and so forth (1 case of obesity and myocardial failure, and 1 of eclampsia); Group 2, 4 cases in which the obstetric treatment was apparently inadequate (3 cases of ruptured

health survey by the American Academy of Pediatrics at the general meeting on the following day

It was moved and seconded that the report of the Committee on Child Health be accepted, the motion was carried

The report of the Committee on the Control of Cancer was then presented by the chairman, Dr George C Wilkins

Last year, the House of Delegates approved a suggestion of this committee that a cancer-instruction day be offered to general practitioners of the State. During April, which is cancer-control month, such a meeting was held at Manchester. A program of thirty-minute talks on the diagnosis and treatment of eight different forms of cancer was presented by five New Hampshire surgeons and three surgeons from Boston. These talks were interesting and stimulating, but the committee received slightly less than one hundred acceptances and some of those accepting did not attend. Furthermore, the men who did attend were mostly the ones who are progressive, well informed and always attend medical meetings. The committee feels a certain amount of disappointment that there were not in attendance more rural and urban general practitioners who see few cancer cases but on whom the fate of a patient with cancer chiefly depends. Your committee intends to plan another meeting next year. The expenses of the meeting, including an excellent lunch, were borne by the Field Army of the American Cancer Society.

Since our last report, two physicians attached to the cancer clinics have taken advantage of the aid given by the Field Army for refresher courses. We hope and expect that more will take advantage of this opportunity, now that so many physicians have returned from the services.

High-school education in cancer control has greatly increased. Last year, the schools in Manchester, where the experiment was initiated, asked for its continuance. Last September, with the active co-operation of the Commissioner of Education, the instruction pamphlets and teachers' guides were offered to all the high schools of the State. At the present time, over 60 per cent of the high schools are using the instruction pamphlets in the science classes. This development has been the responsibility of the Field Army, aided by your committee.

The Cancer Commission and its fourteen clinics have continued to function smoothly. Some clinics have few patients and some have many, but it has been found that the usefulness of a clinic depends chiefly on the interest, ability and enthusiasm of its director. During the past year, 1441 patients attended the clinics, of whom 592 were new patients and 849 were making return visits. Of the new patients, 51 per cent were found to have cancer.

There is continued evidence of the need of public education in the early signs of cancer, and of the value of early treatment, especially among people of the middle and older ages. The younger generation accept it more readily, and therein lies our hope of good results from continual educational efforts.

Your committee sent three short letters to all physicians in the State. One, entitled "Breast Tumors," urged the removal of all definite tumors of the breast and cited tumors as small as 5 mm that were definitely malignant. In the presence of breast tumor one should never advise "let it alone." Another letter discussed "The Significance of a Negative Biopsy Report," and explained why and how errors could be made. It was suggested that in all questionable cases a conference between the surgeon and the pathologist is always advisable. Our last letter described the usual locations of skin cancer, the usual types found, and suggestions regarding diagnosis and treatment, particularly stressing that any new growth on the skin of a patient over forty years of age should be considered malignant until proved otherwise.

Your committee recommends increasing the Committee on the Control of Cancer to five members and asks the House of Delegates to instruct the Nominating Committee to add two names.

Your committee has expended the entire amount appropriated last year. On account of the increased cost of printing and a larger number of physicians, we request the sum of \$60.00 for next year's expenses.

GEORGE C WILKINS, Chairman
RALPH E MILLER
GEORGE F DWIGELL

Dr Lewin, for the Committee on Officers' Reports, recommended that the Committee on the Control of Cancer be increased to five members. This motion was duly seconded.

Dr Dye expressed the opinion that his committee would be in agreement that Section 11 of Chapter VIII of the by-laws be amended and that the Committee on the Control of Cancer be increased to five members, and therefore moved that this recommendation be laid on the table, to be voted on at the meeting on the following morning.

This motion was duly seconded and was carried.

Dr Lewin, for the Committee on Officers' Reports, moved that the sum of \$60.00 for the Committee on the Control of Cancer be approved. This motion was duly seconded and was carried.

Dr Lewin, for the Committee on Officers' Reports then moved that the report of the Committee on the Control of Cancer be accepted and that Dr Wilkins be commended for his unceasing efforts to improve cancer diagnosis and treatment throughout the State. This motion was duly seconded and was carried.

The report of the Committee on Maternity and Infancy was then read, as follows:

Each year the Committee on Maternity and Infancy of the New Hampshire Medical Society conducts a study on the maternal deaths, infant deaths and stillbirths reported for the calendar year previously ended. This study is for mortality reported for the year 1945. As in the past, the committee has endeavored to obtain as full data as possible on each death, analyze, and so far as possible appraise and come to conclusions on the material submitted by physicians in their answers to questionnaires. It should always be borne in mind that infallible judgment is impossible and that conclusions drawn are to be interpreted in the light of objective observers looking into a situation after the event has passed and, in retrospect, appraising the conduct entering into the final result. The committee wishes to stress the fact that conclusions drawn are accurate only to the degree that data at hand are complete. Sometimes the information on a given case is scanty indeed and it is urged that physicians and hospitals make a special effort to submit information as complete as possible.

It is planned that another year the committee will submit a more complete questionnaire designed to secure as full data as possible. It is hoped that such a device will aid greatly in making the study more complete.

The information for the study was gathered from the records of physicians and hospitals. All but one physician responded to the questionnaires, most cases having been reported with fair completeness. Assistance in gathering and compiling data was obtained through personnel of the State Department of Health, and as in the past the committee did not know the identity of the physician, patient or hospital when evaluating the facts presented by their agent.

The year 1945 was gratifying in that the maternal death rate decreased from that of the two previous years. The lowest rate was in 1942 1.6 per 1000 live births. The rate in 1945 was 1.9 per 1000 live births. The number of ma-

program would be inefficient and ineffective, as well as detrimental to the best interests of patients. If government participation on the economic side of medical care is necessary through the establishment of any form of compulsory insurance, we favor the utilization of existing non-profit insurance programs under the sponsorship of medical societies, government funds being used only to pay the premiums for the insured persons. The President is discussing this problem with the county societies throughout the year, and has actively registered his opposition to the Wagner-Murray-Dingell Bill through communication with the appropriate members of Congress and government officials.

New Hampshire Physicians' Service

Gratifying progress in growth has been made throughout the last year. There are now 36,000 participants in the Surgical Division, of whom 6000 are also covered under the Medical Division. This represents a fourfold increase over the enrollment a year ago.

Financially, the Corporation has accumulated sufficient reserves to permit the repayment of the original capital loan and the extension of coverage under both the surgical and medical contracts, with a reduction of the premium for the medical contract.

Studies are now being made on the coverage of veterans care under a contract with the Veterans Bureau — a program already in effect in some other states — and on the coverage of indigent cases under a contract with the State Board of Public Welfare. Such coverage would materially increase the usefulness of the Service and would provide a valuable example of the possibility of co-operation in medical care between the government and the medical profession, with the control of the medical aspects remaining in the hands of the medical profession.

The whole-hearted co-operation of the members of the New Hampshire Medical Society in most areas of the State has been the key factor in the success of the Blue Shield program. Seventy-five per cent of the members are enrolled as participating physicians, the county enrollments running from 48 per cent to 98 per cent, seven counties have over 80 per cent enrollment. We need, however, the co-operation of the other 25 per cent to make the service fully effective. It is interesting to note that men returning from the armed forces are rapidly signing up as participating physicians. Constructive criticism has been helpful and has been gratefully accepted by the trustees of the New Hampshire Physicians' Service. Your committee wishes to commend the members of the New Hampshire Medical Society for their co-operation.

National Physicians' Committee

The National Physicians' Committee has organized a vigorous campaign against the Wagner-Murray-Dingell Bill, which undoubtedly has had considerable effect in arousing opposition throughout the nation. For this reason, the majority of your committee urges the New Hampshire Medical Society collectively and individually to support the National Physicians' Committee by encouragement and by financial aid.

The chairman is compelled to render a minority report in opposition to the methods employed, believing that the dogmatic propaganda broadcast by the National Physicians' Committee, employing on occasion apparently deliberate distortion and misrepresentation, will in the long run do a distinct disservice to the medical profession by cheapening the cause of medicine and by alienating the sympathies of the thoughtful layman.

Blue Triangle

The proposal of the New Hampshire Bankers' Association for physician-secured loans to patients for the payment of their medical bills was referred to the committee by the last House of Delegates. Your committee believes it is inadvisable to sponsor this proposal inasmuch as the Blue Triangle emblem of the plan would cause confusion with the Blue Shield and Blue Cross, and the plan itself to a certain degree would work at cross purposes with the voluntary insurance program.

L. K. SYCAMORE, *Chairman*
FRANCIS J. C. DUKE
R. W. ROBINSON

Dr Lewin, for the Committee on Officers' Reports, stated that a new and interesting approach to government participation in medical care had been brought out by the Committee on Medical Economics. If the Government must participate in medical care, it should do so only to the extent of paying the premiums for the insured persons in some prepayment-insurance program under the sponsorship of medical societies. This would be good only if participation ended there. Dr Lewin asked for discussion on whether there was agreement or disagreement with the Taft Bill as presented and whether the Government would co-operate in a prepayment plan under medical society sponsorship. He moved that the Society go on record as favoring government participation in a prepayment-insurance program under medical-society sponsorship. This motion was duly seconded.

The President, who had been in some measure associated with the development of this voluntary insurance plan in New Hampshire for some years, stated that his opinions had gone through all phases. Certainly, if the Government were to participate in this program, the only proper method was the supplying of the necessary means to cover the care given patients. The voluntary plans sponsored in the various states appeared to be the best course. He feared a very dangerous attack on the whole of the relation between patient and physician that any type of insurance or any agent assuming the cost of medical care for the patient might bring about. He pointed out that a patient must be required to make some sacrifice. He considered the local, voluntary plans much better than any compulsory insurance plan administered by anything as remote as the federal government.

In a small state like New Hampshire, the problems were close enough together for members of the professional committees of Blue Shield to regard the Blue Shield as the agent of the physician, consequently there was a definite reason for protecting it, to make its insurance successful. The President recalled a discussion two years previously regarding federal participation in medicine and whether it was impossible for the Government to collect moneys by taxation or otherwise and then to use the money for voluntary plans of insurance. The Government appeared to be interested in such a scheme.

The President further pointed out that one of the major objectives of interest in the voluntary-insurance plan was to provide some way not only of taking care of the medically indigent but also of devising a fee schedule to furnish some recompense at a time when the burden was tremendous. There had been a good deal of dissatisfaction with the system of treating the indigent under that fee schedule, which had been modified once. The President had had some discussions with the State Board of Welfare during the previous year and had suggested the State pay the insurance premium for indigent care,

uterus, and 1 of post-partum hemorrhage), Group 3, 7 deaths that were apparently unavoidable (3 cases of eclampsia, and 4 of pulmonary emboli), and Group 4, 2 cases in which data were insufficient and the cause of death was therefore undetermined (1 case of postoperative pulmonary emboli, and 1 of myocardial failure).

In 1 case in Group 3 in which the cause of death was reported as post-partum hemorrhage, the committee believed that treatment was inadequate. The patient went into shock following a cesarean section, and no intravenous therapy, particularly plasma, was administered for at least forty-five minutes, although the anesthetist was aware of the patient's condition. The committee considered the cause of death to be surgical shock rather than post-partum hemorrhage, especially since there was no evidence of excessive bleeding. It was further believed that an anesthetist should take the initiative in ordering shock therapy, especially when the attending physician has his hands full with delivery or surgery.

Maternal mortality rates per 1000 live births by years were as follows: 1933, 6.3, 1934, 5.4, 1935, 6.1, 1936, 4.8, 1937, 4.3, 1938, 3.8, 1939, 3.1, 1940, 3.1, 1941, 1.9, 1942, 1.6, 1943, 2.4, 1944, 2.9, and 1945, 1.9.

The deaths by counties in 1945 were Belknap, 1, Hillsborough, 6, Strafford 5, Coos 2, Cheshire 1, and Rockingham 1.

INFANT DEATHS

The following is a list of the ten chief causes of death recorded for infants under one year of age. In 1945 there were 299 deaths from all causes — a rate of 35 per 1000 live births. In order, the causes were prematurity, congenital malformations, birth injuries, other diseases peculiar to first year of life, lobar pneumonia, pneumonia (other), accidental suffocation, diarrhea and cerebrospinal meningitis. It should be noted that the chief cause of death listed is premature birth. The Committee believes that this should not be considered a cause of death and that better and more adequate treatment and facilities for the care of premature infants should be stressed. Maintenance of body temperature and thorough nursing care, including proper feeding, is essential.

STILLBIRTHS

In 1945 200 stillbirths were reported — a rate of 23.4 per 1000 live births. The causes were varied and substantially unrevealing. Again the committee prints the accepted definition of a stillbirth, as follows: "A fetus showing no evidence of life after complete birth (no action of heart, breathing or movement of voluntary muscle), if the twentieth week of gestation has been reached, should be registered as a stillbirth." For the most part the causes of fetal death as given on death certificates are maternal conditions, with the exception of fetal deformities. Here again the classification of causes of stillbirths varies. The International Commission for Revision of the International List of Causes of Death in 1938 adopted the following classification, which is given here in outline only: stillbirth caused by disease in, or accident to, the mother, anomalies of the fetus, placenta or cord, death of the fetus from injury or other causes, and stillbirth due to other causes. In a diagnosis of causes of death, the foregoing should be kept in mind.

COMMENTS AND RECOMMENDATIONS

By way of summary and to emphasize examples of apparently poor obstetrics the committee wishes to point out the following facts and make some suggestions. It is hoped that the conduct of future deliveries may be favorably affected by constructive criticism. The cases of toxemia reported again illustrate that there is still a tendency to neglect the medical aspects of the condition by inadequate treatment. The majority of patients with toxemia reported this year were seen late in pregnancy, with symptoms of the toxemia apparent. The tendency has been to induce labor or perform a cesarean section without giving adequate medical care or preparation. The committee strongly urges the immediate treatment of toxemia by the use of magnesium sulfate in the early stages, early induction with due regard to prematurity, glucose and magnesium sulfate in severe cases and in eclampsia

complete digitalization as soon as possible, with added use of glucose and oxygen if necessary. The magnesium sulfate, glucose and digitalization should be instituted immediately, pending the decision of the method or time of delivery. It is more important that the patient be treated than to empty the uterus.

The committee wishes to make a plea for a larger number of trained and skilled anesthetists. Many unfortunate incidents can be avoided if a trained anesthetist is constantly alert for symptoms of shock and is skilled in the administration or supervision of shock therapy. Almost every year a case is cited in which the failure of the anesthetic to act quickly or adequately leads to the patient's death.

It is urged that more autopsies should be sought. Frequently the correct diagnosis can be determined, especially in cases in which the cause of death is recorded as post-partum hemorrhage or shock. Post-partum hemorrhage may be due to retained cotyledons, ruptured uterus, cervical tears, fibromas and varicosities.

If hemorrhage is suspected, immediate search for such causes should be instituted. The committee emphasizes again the necessity of proper diagnosis and immediate treatment of patients with hemorrhage or who show signs of shock immediately or soon after delivery, whether delivery was spontaneous or operative. Plasma, now available to all free of charge, should prove an invaluable means of combating shock in such cases.

It is again stated that the committee cannot find justification for a forced delivery. In cases of transverse presentation it is possible that an external cephalic version could be attempted before labor has set in, and if the membranes are intact, the patient should surely be permitted to go to full dilatation before delivery is attempted. If the membranes have ruptured, the cervix is not dilated and the uterus is dry, an internal podalic version is definitely contraindicated. A better alternative is cesarean section.

The committee wishes to comment on the value of qualified consultation in obstetrics emphasizing that the consultant's prerequisites should include ample experience in obstetrics and not merely skill in surgery.

If the committee is to make fair and helpful suggestions, based on conclusions reached in this study, it is essential that better reporting of the facts be practiced by physicians, since the committee has nothing to go on except information submitted.

The committee wishes to thank physicians and hospitals for reports completely and painstakingly filled out, as well as all physicians who co-operated in preparing this report. Acknowledgment and thanks are also expressed to the State Department of Health for its aid in compiling data and furnishing personnel.

ROBERT O. BLOOD, *Chairman*
BENJAMIN P. BURPEE
MARION FAIRFIELD

Dr. Lewin, for the Committee on Officers' Reports, commended the work of the Committee on Maternity and Infancy and moved that the report be accepted. This motion was duly seconded and was carried.

The report of the committee on Medical Economics was then presented by the Chairman, Dr. L. K. Sycamore, as follows:

For the last year, your committee has functioned mainly in the separate activities of its members, one of whom is president of the New Hampshire Medical Society, the chairman being president of the New Hampshire Physicians' Service. These activities occupied the time of the members to such an extent that any further functioning of the committee as a whole did not seem possible. Your committee has, however, considered the following subjects and presents its conclusions in this report:

Wagner-Murray-Dingell Bill

Your committee opposes the method of distribution of medical care proposed in the bill, believing that such a

program would be inefficient and ineffective, as well as detrimental to the best interests of patients. If government participation on the economic side of medical care is necessary through the establishment of any form of compulsory insurance, we favor the utilization of existing non-profit insurance programs under the sponsorship of medical societies, government funds being used only to pay the premiums for the insured persons. The President is discussing this problem with the county societies throughout the year, and has actively registered his opposition to the Wagner-Murray-Dingell Bill through communication with the appropriate members of Congress and government officials.

New Hampshire Physicians' Service

Gratifying progress in growth has been made throughout the last year. There are now 36,000 participants in the Surgical Division, of whom 6000 are also covered under the Medical Division. This represents a fourfold increase over the enrollment a year ago.

Financially, the Corporation has accumulated sufficient reserves to permit the repayment of the original capital loan and the extension of coverage under both the surgical and medical contracts, with a reduction of the premium for the medical contract.

Studies are now being made on the coverage of veterans' care under a contract with the Veterans Bureau — a program already in effect in some other states — and on the coverage of indigent cases under a contract with the State Board of Public Welfare. Such coverage would materially increase the usefulness of the Service and would provide a valuable example of the possibility of co-operation in medical care between the government and the medical profession, with the control of the medical aspects remaining in the hands of the medical profession.

The whole-hearted co-operation of the members of the New Hampshire Medical Society in most areas of the State has been the key factor in the success of the Blue Shield program. Seventy-five per cent of the members are enrolled as participating physicians, the county enrollments running from 48 per cent to 98 per cent, seven counties have over 80 per cent enrollment. We need, however, the co-operation of the other 25 per cent to make the service fully effective. It is interesting to note that men returning from the armed forces are rapidly signing up as participating physicians. Constructive criticism has been helpful and has been gratefully accepted by the trustees of the New Hampshire Physicians' Service. Your committee wishes to commend the members of the New Hampshire Medical Society for their co-operation.

National Physicians' Committee

The National Physicians' Committee has organized a vigorous campaign against the Wagner-Murray-Dingell Bill, which undoubtedly has had considerable effect in arousing opposition throughout the nation. For this reason the majority of your committee urges the New Hampshire Medical Society collectively and individually to support the National Physicians' Committee by encouragement and by financial aid.

The chairman is compelled to render a minority report in opposition to the methods employed, believing that the dogmatic propaganda broadcast by the National Physicians' Committee, employing on occasion apparently deliberate distortion and misrepresentation, will in the long run do a distinct disservice to the medical profession by cheapening the cause of medicine and by alienating the sympathies of the thoughtful layman.

Blue Triangle

The proposal of the New Hampshire Bankers' Association for physician-secured loans to patients for the payment of their medical bills was referred to the committee by the last House of Delegates. Your committee believes it is inadvisable to sponsor this proposal inasmuch as the Blue Triangle emblem of the plan would cause confusion with the Blue Shield and Blue Cross, and the plan itself to a certain degree would work at cross purposes with the voluntary insurance program.

L. K. SYCAMORE, Chairman
FRANCIS J. C. DUBE
R. W. ROBINSON

Dr Lewin, for the Committee on Officers' Reports, stated that a new and interesting approach to government participation in medical care had been brought out by the Committee on Medical Economics. If the Government must participate in medical care, it should do so only to the extent of paying the premiums for the insured persons in some prepayment-insurance program under the sponsorship of medical societies. This would be good only if participation ended there. Dr Lewin asked for discussion on whether there was agreement or disagreement with the Taft Bill as presented and whether the Government would co-operate in a prepayment plan under medical society sponsorship. He moved that the Society go on record as favoring government participation in a prepayment-insurance program under medical-society sponsorship. This motion was duly seconded.

The President, who had been in some measure associated with the development of this voluntary insurance plan in New Hampshire for some years, stated that his opinions had gone through all phases. Certainly, if the Government were to participate in this program, the only proper method was the supplying of the necessary means to cover the care given patients. The voluntary plans sponsored in the various states appeared to be the best course. He feared a very dangerous attack on the whole of the relation between patient and physician that any type of insurance or any agent assuming the cost of medical care for the patient might bring about. He pointed out that a patient must be required to make some sacrifice. He considered the local, voluntary plans much better than any compulsory insurance plan administered by anything as remote as the federal government.

In a small state like New Hampshire, the problems were close enough together for members of the professional committees of Blue Shield to regard the Blue Shield as the agent of the physician, consequently there was a definite reason for protecting it, to make its insurance successful. The President recalled a discussion two years previously regarding federal participation in medicine and whether it was impossible for the Government to collect moneys by taxation or otherwise and then to use the money for voluntary plans of insurance. The Government appeared to be interested in such a scheme.

The President further pointed out that one of the major objectives of interest in the voluntary-insurance plan was to provide some way not only of taking care of the medically indigent but also of devising a fee schedule to furnish some recompense at a time when the burden was tremendous. There had been a good deal of dissatisfaction with the system of treating the indigent under that fee schedule, which had been modified once. The President had had some discussions with the State Board of Welfare during the previous year and had suggested the State pay the insurance premium for indigent care,

at that time the President had stated that this presented simply one attitude. The medical profession had apparently agreed that this fee schedule was better than nothing, and that it was adequate recompense for the services rendered, provided that the State paid for the care. He pointed out, however, that physicians were selling their services to the State, for the care of the indigent, for a sum considerably less than the actual worth of those services, and that physicians must protect themselves and their ideals. There was no reason for the medical profession to give its service at a moderate fee, or at a cost lower than that of the grocer or other people dispensing commodities paid for by the State. Of course, laboratory and similar fees had not been included in the insurance plan, but it had been thought that such fees could be adjusted in the insurance scheme by accepting a type of service policy, including a complete service, the fees of the physician being kept on a detailed record form.

The President further stated that every case did not agree with Dr. Sycamore's minority report condemning the National Physicians' Committee.

Dr. Wilkins objected to the suggestion that the Society approved government participation in health insurance.

Dr. Lewin accepted the objection as an amendment.

The Secretary stated that in anticipation of this discussion he had sent a telegram to the American Medical Association asking its attitude on such pro-

posals as the Taft Bill, and that the American Medical Association had replied that such proposals had not yet been considered officially. The Secretary questioned whether the House of Delegates should make any decision until the policy of the American Medical Association was known.

Dr. Clough agreed that decision on the program should be postponed, pending the opinion of the American Medical Association. Since the Blue Shield had been created to combat any interference by the Government in the practice of medicine in New Hampshire, Dr. Clough believed that it would be wiser to say nothing for the present but to consider the matter at greater length.

Dr. Ladd stated that if the motion were passed as read, the sponsors of the Wagner-Murray-Dingell Bill would at once say that the State of New Hampshire favored their bill. He therefore agreed that the wisest course was not to take any action until the attitude of the American Medical Association had been determined. He moved that the motion be laid on the table. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, moved that the House of Delegates not sponsor the Blue Triangle Plan of the New Hampshire Bankers' Association. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, then moved that the report of the Committee on Medical Economics be accepted. This motion was duly seconded and was carried.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 32341

PRESENTATION OF CASE

A forty-seven-year-old shipping clerk entered the hospital because of chronic cough

The patient had been in apparent good health until a year before entry when he developed a non-productive cough, which he at first attributed to an upper respiratory infection but which persisted throughout the winter and became worse in the spring, with the development of some mucoid sputum. A physician prescribed pills that controlled the cough fairly well until the time of admission. The sputum had never contained blood or pus, and the patient denied any real pain, although he had some suprasternal and substernal soreness. He had noted no fever, but was told by his physician that he ran a slight temperature. Since the beginning of the illness he had lost 65 pounds, although his appetite had remained good.

Physical examination revealed a 2.5-cm rubbery, superficial lymph node in the right supraclavicular region, just beneath the edge of the platysma muscle, and several deeper nodes in the right supraclavicular region. The heart and lungs were completely normal. Examination of the abdomen was negative, and the liver edge could not be made out. The prostate was slightly enlarged.

The temperature was 99.8°F, the pulse 85, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 13 gm and a white-cell count of 9000. The urine was normal.

An x-ray film of the chest showed the left hilus to be low and surrounded by a homogeneous area of increased density, with irregular flame-like borders (Fig 1). In the lateral view the density was seen to occupy the hilar area. There were increased lung markings in the region of the left lower lobe and in the base of the left upper lobe, probably representing atelectatic areas. The right lung field was clear, except for a thin linear area of increased density, which probably represented minimal atelectasis. The diaphragm was normal in position, and both costophrenic angles were clear. The heart and upper mediastinum were not remarkable.

A biopsy of the right supraclavicular node and a bronchoscopy were performed.

DIFFERENTIAL DIAGNOSIS

DR. BRIANT L. DECKER: May we see the x-ray films?

DR. JAMES R. LINGLEY: This film shows the enlargement of the left hilus that is described in the record, and in the lower portion a lobular mass can be seen. The lateral view shows the density in the region of the hilus, which I believe definitely involves the base of the upper lobe and probably of the lower lobe. The right lung is clear except for this small area of atelectasis. There is no displacement of the heart, no mediastinal enlargement, and no fluid.

DR. DECKER: Is there any collapse in the left lower lobe?

DR. LINGLEY: I think that there is probably some collapse in both lobes.

DR. DECKER: Is there any calcification?

DR. LINGLEY: No.

DR. DECKER: Is this shadow a node?

DR. LINGLEY: No, I believe that it is the transverse process of a vertebra.

DR. DECKER: This forty-seven-year-old shipping clerk had had chronic cough for two years, with only mucoid sputum, and had lost 65 pounds. He had no real chest pain but had substernal soreness and slight fever. Enlarged lymph nodes were found in the right supraclavicular region on physical examination, and there were the x-ray findings that Dr. Lingley has pointed out. I assume that the two processes — that is, the x-ray appearance and the enlarged nodes — were related. Consequently I believe that this was some type of new growth. The two most probable diagnoses are primary bronchiogenic carcinoma and lymphoma, although I lean more strongly toward carcinoma. With lymphoma of this duration one would see a mediastinal mass and would find lymph nodes in the axillas and elsewhere. I believe that when invasion of the lung occurs with lymphoma it is fairly advanced, although it may occur early on rare occasions. The weight loss could go with either condition. If it were associated with carcinoma, I should expect more extensive carcinoma than was apparent in this case. The slight temperature could also go with either. From the x-ray appearance I believe that this lesion, which caused partial obstruction of bronchi, together with metastases, was most probably an adenocarcinoma. Small-cell carcinoma usually grows much more rapidly but it does spread by the lymphatic vessels. A year, however, is too long a duration for such a tumor. Squamous-cell or epidermoid carcinoma is directly invasive and usually does not involve the lymph nodes. Adenocarcinoma travels by the blood stream, is often found in the lymphatic vessels, and frequently produces distant metastases. It is perhaps more slowly growing than

a small-cell carcinoma I am most in favor of adenocarcinoma

Tuberculosis, which could have produced this picture, is unlikely in a person of this age. Lymph nodes and a process of this sort could occur in a young person or in an older patient, with more extensive tuberculosis.

Sarcoid is also a possibility, although I do not believe that so much weight loss would have been noted. Sarcoid is usually bilateral and symmetrical.

The various mycoses are unlikely because the patient's occupation did not expose him to the agents that cause such diseases — he was a shipping

DR MALLORY Dr Miller, will you tell us what you know about the case?

DR CARROLL MILLER I saw this man in my office before I sent him to the hospital, and at that time he brought with him x-ray films that had been taken elsewhere. The ray formation from the central hilar mass was more marked in those plates than in the ones taken in this hospital. In both supraclavicular fossae there were nodes that were fixed, firm and rather matted together, and I believed that the diagnosis was carcinoma of the lung, with metastases to the supraclavicular fossae, although we have seen few carcinomas of the lung that

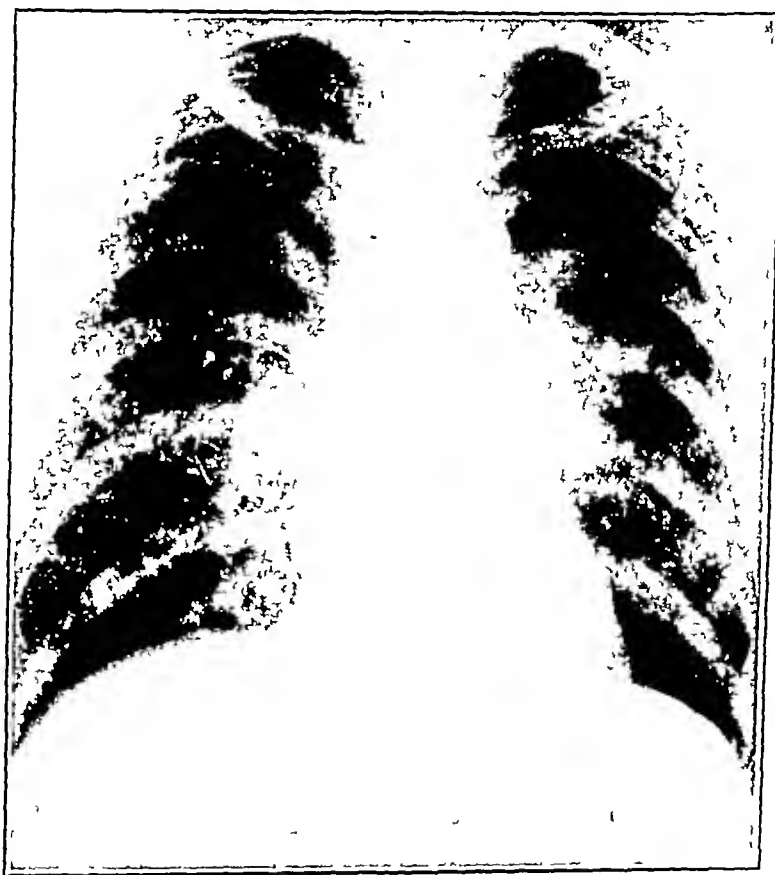


FIGURE 1 Roentgenogram of Chest

clerk. He did not come from the Southwest, so that coccidioidal granuloma can probably be ruled out. In a chronic stage the other mycoses would have been more ulcerating, with lesions of the skin.

In conclusion I believe that this was most probably an adenocarcinoma, primary in the bronchus.

DR TRACY B. MALLORY Are there any other suggestions?

DR. DONALD C. KING Dr Sweet and I have just been talking it over, but we do not agree that adenocarcinoma is a likely diagnosis. If this was a carcinoma we believe that it was probably epidermoid

metastasized in a relatively early stage to that region, such cases do occur. Because of the weight loss, the time interval and the x-ray appearance my diagnosis was carcinoma. I think that the bronchoscopic findings were interesting and similarly confusing.

CLINICAL DIAGNOSIS

Carcinoma of lung

DR DECKER'S DIAGNOSIS

Primary bronchiogenic adenocarcinoma

ANATOMICAL DIAGNOSIS

Tuberculosis of bronchus

PATHOLOGICAL DISCUSSION

DR MALLORY On bronchoscopic examination a tumorlike outcropping was seen on the bronchial wall. The bronchoscopist also considered the appearance characteristic of carcinoma. The surprise came in the microscopic examination. The biopsy from the bronchus showed tuberculous granulation tissue, and that of the supraclavicular lymph node also showed frank caseous tuberculosis. The patient is now in a sanatorium.

CASE 32342

PRESENTATION OF CASE

A thirty-one-year-old housewife entered the hospital because of lower abdominal pain.

The patient had apparently been in good health until six weeks before entry, when she experienced crampy lower abdominal pains associated with the menstrual period. The pains were dull and aching and radiated to both sides of the lower back. The period had begun at the usual time, but bleeding was scanty and prolonged over ten days. The periods usually occurred every twenty-eight days, lasted four or five days and required about four pads. They were never accompanied by discomfort. After this period had ended, the patient continued to suffer from intermittent attacks of similar pain. The following period came at the expected time but lasted only two days, with scanty flow. Four days before entry, about an hour after supper, the pain became markedly worse, and the patient vomited her supper. The pain continued during the night, and she vomited several more times, producing whitish "phlegm and water." Her condition remained essentially unchanged, and she continued to vomit, despite taking only fluids by mouth. Two days before entry she felt somewhat improved, vomiting only once and taking some solid food. On the day of admission, however, the pain was severer than at any previous time and she again began to vomit. At no time did the vomitus contain bile, blood or coffee-ground material. She had had no bowel movement and little or no flatus during the four days before entry. Since the onset of the illness she had had sharp lower midline abdominal pain during urination, but passage of the urine itself caused no burning and the urine was not bloody. She had felt feverish during the illness but had had no chills. During the week before entry she had had a "slight cold," with rhinitis and some coughing.

The patient had four children aged twelve, ten, six and four years. Seven years previously she had had a miscarriage, and since the birth of her young-

est child she had noticed a scant whitish discharge. Both the patient and her husband denied any venereal infection.

Physical examination revealed a well developed woman who appeared acutely ill. The heart and lungs were normal. The abdomen was distended, with diminished peristalsis and some fullness in the suprapubic region. There was diffuse and rebound tenderness, most marked in the lower abdomen, especially in the midline. Pelvic examination showed a grapefruit-sized tender mass in the left vault lying laterally and anteriorly. There was no tenderness on moving the cervix.

The temperature was 99°F, the pulse 105, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

Examination of the blood revealed a red-cell count of 2,620,000, with 7.7 gm of hemoglobin, and a white-cell count of 8900, with 74 per cent neutrophils. The corrected sedimentation rate was 66 mm per hour. The chloride was 101 milliequiv per liter, and the total protein 6.2 gm and the non-protein nitrogen 18 mg per 100 cc. A blood Hinton test was negative. The urine was normal.

A plain film of the abdomen showed only a considerable amount of gas and fecal material retained in the colon, as well as gas in what appeared to be several loops of small intestine. The pelvis was filled by a homogeneous mass of increased density that was consistent with a full bladder.

Cultures of the cervix were negative for gonococci.

On the evening of the first hospital day the temperature rose to 99.8°F, and the patient was placed on sulfadiazine and penicillin. On this regime the mass felt by vaginal examination seemed to be decreasing in size and was definitely confined to the broad ligament. The subjective symptoms also subsided until the sixteenth hospital day, when the pain in both lower quadrants returned. On the twenty-first hospital day a peritoneoscopy revealed a questionable cyst of the right ovary. On the twenty-sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR JOHN B. MCKITTRICK This thirty-one-year-old mother of four children, previously in excellent health, entered the hospital with the complaint of lower abdominal pains of six weeks' duration. The pains which were first noted in association with a menstrual period, were dull and aching and radiated to both sides of the lower back. The period had started in a perfectly normal fashion except that bleeding was scanty and prolonged for ten days, this was distinctly unusual, since the patient had never had discomfort with her periods and the menses had usually lasted four or five days. The amount of flow was abnormal, as were the duration and, of course, the pain. When the actual menstrual flow had ceased, the pain continued in an intermittent fashion but apparently did not change in

character. The next period came at the proper interval but was abnormal in that it lasted only two days and the flow was again scanty. This second menstrual period apparently occurred about two weeks before admission to the hospital. Four days before admission, shortly after supper, the pain became much severer and more protracted and was accompanied by repeated vomiting throughout the night of food recently eaten. Two days later the patient improved somewhat. The vomiting was less persistent, and she was able to take a small amount of solid food. On the day of admission, however, there was a sharp recrudescence of the pain and vomiting also returned, at all times the vomitus was free of blood and bile. During this four-day period, during which the symptoms had altered and become severer, a new element was introduced, namely, absence of bowel movements associated with the passage of little or no flatus. Another symptomatic clue is that during the course of the illness the patient had sharp discomfort on urination, but the passage of urine was not associated with burning and the urine was apparently normal. The patient stated that she had had no chills during the course of her illness but at times had felt feverish.

It seems clear that some acute process was going on and was localized to the abdomen and associated with the genital system. What could have caused such an abrupt change in the menstrual cycle, associated with low abdominal pain radiating through to the back and with involvement of the intestinal tract in a way that interfered with intestinal motility? Several things come to mind. Was this an inflammatory process? The patient felt feverish but had no chills. Beyond that there is no indication of how prostrated she had been by the illness. It is perfectly conceivable that pelvic inflammatory disease could persist for six weeks, becoming acute, involving the intestinal tract, — usually the small bowel, — and causing intestinal obstruction. As a rule, however, such patients are rather acutely ill, with a high fever, they frequently have chills, and when the process is as acute as this seemed to be, there is usually associated urinary symptomatology. Acute appendicitis, which frequently causes this type of abdominal pain and low-grade fever, must be considered. A patient may present such a history of several weeks' duration and may consult a physician only when symptoms become much severer as in the case under discussion. Was this a benign tumor, such as an ovarian cyst, that during a period of six weeks was intermittently and finally irreducibly twisted and caused the acute symptomatology for the last four days before admission? Such a tumor is rather unlikely, although most of the symptoms could be explained on that basis. As a rule, ovarian cysts do not cause the disturbance in the menstrual cycle that occurred in this case. They cause nausea and vomiting, as well as the type of pain that the patient complained of,

but not usually the degree of disturbance in intestinal motility that was apparently present. I think that one need mention malignant tumor only to be complete, but there was no evidence that this process was anything but acute. By a process of rapid elimination one arrives at the diagnosis that seems to fit this whole problem best — namely, some type of extrauterine pregnancy which could account for the change in the menstrual history, as well as the pain and the intestinal symptoms.

On admission to the hospital the patient was well developed and acutely ill. Physical findings were limited to the abdomen, which was distended. There were diminished peristalsis and suprapubic fullness. Diffuse tenderness and rebound tenderness were most marked in the lower abdomen, near the midline. Pelvic examination showed a grapefruit-sized tender mass lying to the left and anteriorly. There was no tenderness on moving the cervix. The temperature was 99°F, the pulse 105, and the respirations 20. The blood pressure, I am interested to note, was normal. Examination of the blood showed a red-cell count of 2,600,000, with a hemoglobin of 7.7 gm, and a normal white-cell count, with 74 per cent neutrophils, the corrected sedimentation rate was 66 mm per hour. Other studies, including the chloride, protein and nonprotein nitrogen levels and the blood Hinton reaction, were negative. Examination of the urine was also negative. A plain film of the abdomen confirmed the clinical impression of an excessive amount of retained gas and fecal material in both the large and the small bowel — primarily the former — and in addition revealed the mass palpated by the examiner, which was interpreted as being consistent with a full bladder. Apparently there were no characteristic features about this mass, but that is not surprising. Cultures of the cervix were negative for gonococci. The record does not give a vital bit of information that I am sure was determined: the results of the test for pregnancy. I do not see how one could examine this patient and listen to her history without considering that question.

In summary, this patient was acutely ill, with a mass in the pelvis, an altered menstrual cycle, and evidence of intestinal dysfunction but little suggestion of an acute inflammatory process — certainly not an inflammatory process that was causing much of a systemic reaction. The temperature was only slightly elevated, and the white-cell count was normal, although there was an elevated sedimentation rate, the upper limit of normal in this hospital being 20 mm. Just what does that mean? It is perfectly true that in some cases the sedimentation rate is elevated out of proportion to other evidences of inflammation, such as the temperature and the white-cell count, in the presence of venereal infection in the pelvic organs, and it is entirely possible that this patient had such an infection despite the negative culture and the absence of other symptoms.

usually associated with acute pelvic inflammatory disease. The sedimentation rate, however, cannot be depended on to differentiate pelvic inflammatory disease and acute appendicitis. I have mentioned acute appendicitis, and I cannot completely exclude it as the cause of the trouble. The degree of ileus I say "ileus" rather than obstruction because the distribution of the gas shadows was mostly in the large bowel, and at any rate there was certainly no small-bowel obstruction) is entirely consistent with an appendiceal abscess, as were the pain and vomiting. The unusual position of the mass — on the left and anteriorly — and the change in menstrual rhythm are strong evidence against appendiceal abscess. The presence of pelvic inflammatory disease might also account for what I believe to have been an extrauterine pregnancy. Pathologic changes that occur in the tubes following inflammatory disease predispose a patient to such difficulties. On the basis of the way the patient was handled in the hospital, I assume that the condition was considered to be acute pelvic inflammatory disease with probably a tubo-ovarian abscess, since she was treated conservatively until the twenty-sixth hospital day, when she was operated on, the negative culture from the cervix does not exclude pelvic inflammatory disease. If the diagnosis had been extrauterine pregnancy, operation would probably have been performed somewhat earlier. Despite the delay in operation, however, I believe that extrauterine pregnancy offers the best explanation for the anemia, the mass, the ileus, the absence of symptoms referable purely to infection and the change in menstrual cycle. I also believe that the pregnancy was not tubal but abdominal, possibly either ovarian or located in the broad ligament itself. I exclude tubal pregnancy because it does not, as a rule, persist for such a long time without causing dramatic symptoms when there is rupture and enough bleeding to lower the hemoglobin to 7.7 gm. Apparently the process in this patient had bled, but the bleeding was not sufficiently acute or severe to produce shock, which is almost certain to follow when the tubal pregnancy reaches the stage of rupture into the preperitoneal

cavity. She may have had an element of inflammatory disease, which I think was secondary.

My diagnosis, therefore, is extrauterine pregnancy, probably abdominal, with or without low-grade pelvic inflammatory disease.

CLINICAL DIAGNOSES

Ovarian cyst

Pelvic inflammatory disease?

DR. MCKITTRICK'S DIAGNOSIS

Extrauterine pregnancy, probably abdominal

ANATOMICAL DIAGNOSIS

Abdominal pregnancy

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY. There was only one omission, an unintentional one, from this patient's history. She had had her appendix removed at the age of eighteen. If Dr. McKittrick had known this, one confusing factor would have been eliminated. No Aschheim-Zondek test was ever done, and if the diagnosis of pregnancy was seriously considered, such an impression was not recorded. Opinion first favored pelvic inflammatory disease and then shifted to ovarian cyst. The patient was eventually explored, with the latter as the preoperative diagnosis.

At operation a moderate amount of free blood was encountered when the peritoneal cavity was opened. A large mass was found in the left side of the pelvis posterior to the broad ligament and covered by adherent omentum. When the omental adhesions were freed a cavity was broken into, out of which a fetus measuring 9 cm. in length was extruded. A well developed placenta was adherent to the fimbria of the left fallopian tube. There was considerable old clotted blood in the posterior cul-de-sac. A left salpingectomy was done as the simplest method of dealing with the placental implantation. The pregnancy, however, was definitely extratubal and intra-abdominal, as Dr. McKittrick predicted.

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GRADUATES OF NONAPPROVED MEDICAL SCHOOLS

A LETTER published elsewhere in this issue of the *Journal* calls attention again to the difficulties that graduates of nonapproved schools who served as medical officers during the war are having in obtaining additional medical training, particularly as residents in the hospitals of the Veterans Administration. Any unprejudiced discussion of the problem should be based on facts rather than on assumptions, and it seems necessary to question some of the statements contained in the letter.

In the first place, although the majority of graduates of nonapproved schools may have "really felt the 'call' to medicine," most of them were undoubtedly refused admission to approved schools because

of a premedical training that was judged to be relatively inadequate. This, combined with a medical education that failed to provide facilities comparable with those available in approved schools, places a severe handicap on such graduates, which is the obvious reason why so many of them fail to pass board examinations in the states whose statutes permit them to apply for licensure.

Secondly, state medical examining boards are not "closely regulated and governed by the American Medical Association" each state has its own medical practice act. Nor are the specialty boards "by products" of the American Medical Association. The American Board of Surgery, for example, arose following initial efforts by the American Surgical Association, being finally created by the Advisory Board of Medical Specialties after the field had been approved by the Council on Medical Education and Hospitals of the American Medical Association. This board has thirteen members, only three of whom represent the American Medical Association.

Thirdly, it should be emphasized that practically all graduates of nonapproved schools who recently served as medical officers came from two states, — Illinois and Massachusetts, — since these are the only states that regularly permit such graduates to apply for licensure.

When all is said and done, the problems of the graduates of nonapproved schools practically limit themselves to Illinois and Massachusetts, and at least in the latter, efforts are being made to provide these men with further opportunities. All such graduates are eligible to apply for membership in the Massachusetts Medical Society five years after they have been licensed to practice. The Gallupe Plan, commented on editorially in the April 25 issue of the *Journal*, offers to these men hospital affiliation, it is sponsored by the Massachusetts Medical Society and the Massachusetts Hospital Association and has the approval of the Council on Medical Education and Hospitals of the American Medical Association and of the American College of Surgeons. Finally during the past year the Massachusetts Medical Society has conducted courses of postgraduate medical instruction throughout the Commonwealth that have been open to all physicians. It is true that in Massachusetts there is a distinction between the

raduates of approved and nonapproved schools, on the other hand, the proper authorities appear to be doing all that they can to help the latter in improving their medical training

In any discussion concerning the appointment of graduates of nonapproved medical schools as residents in hospitals of the Veterans Administration, it is essential to differentiate two types of institutions — "hospitals" and "affiliated hospitals." The former are solely under the control of the Veterans Administration, and graduates of nonapproved schools have been accepted as residents in these hospitals. The latter, on the other hand, are run in connection with various medical schools and are in the process of being converted into teaching hospitals for those who are desirous of qualifying for certification by one of the specialty boards. The selection of residents is subject to the approval of a committee representing the affiliated medical school or schools, — the Dean's Committee in Massachusetts — and an attempt is made to select only those men who seem likeliest to pass the examinations of their respective specialty boards on the termination of their training. Many graduates of approved schools in the United States and Canada have been turned down, but at least in Massachusetts, some men who do not so qualify have been accepted. Although existing regulations bar the latter from certification by the majority of specialty boards, there is no doubt that the Dean's Committee will do its utmost to make their certification possible, provided that they creditably complete their residencies.

Although the path of the graduates of nonapproved schools is not easy, it appears that those who have shown industry, professional skill and a desire to better themselves have more opportunities now than ever before.

SELF-DEMAND IN INFANT FEEDING

AN ANCIENT fact has been rediscovered as a new theory in infant feeding and, being put to the test, has again been proved, namely, that babies who are fed when they are hungry are in the main happier than babies who are put to nurse when they are not hungry and are denied nourishment when they ask for it. We are witnessing now, in these matters,

a pleasant swing from a gravely pontifical attitude toward the training of the very young to a rather indulgent point of view, admitting that babies are human beings like, for instance, ourselves.

We may be sure that this so-called "self-demand regime" is a relative innovation only among the more cultured classes and that many babies less fortunately situated in other ways have had certain vital needs attended to more promptly, even if in a less determinedly organized fashion. This particular swing away from the regimentation of infancy that accompanied the birth of the specialty pediatrics was initiated, or at least blessed, by that ardent student of infant behavior, Arnold Gesell.

As early as 1937, Gesell and Ilg¹ expressed themselves on this point as follows:

Superficially it might appear that the self-demand schedule would encourage whims and instability in the child. Exactly the opposite is true. For by individualization of feeding the infant is most directly and most completely satisfied. He is satisfied vegetatively and emotionally. He escapes periods of want, anxiety and distress. The promptness and the certainty of satisfaction cumulatively experienced . . . will nourish that sense of security which is essential to mental health.

Other experimenters in this naturalistic method of feeding babies when they are hungry and not forcing them to eat at other times are presenting the results of their own explorations. Notable among these, Trainham, Pilafian and Kraft,² one of the authors being the mother, allowed a pair of lusty, breast-fed twins to write their own tickets for thirteen long months. The results were eminently satisfactory to the infants, although the mother, at times, found herself producing and serving as many as ten meals in a day. This, however, was an unusual case.

On the whole we must accept the obvious conclusion that the inflexibility of a mathematical attitude has been allowed to prevail much too far in the care of an extremely unmathematical subject. We have fallen into the error of believing that fixed quantities of food of prescribed caloric value must be absorbed by infants of certain weights and ages at regular intervals and in a stated number of minutes. Far better is it that more babies, at least during the early weeks of their infancy, should be allowed to benefit from the examples set by these articulate observers and the host of more humble infant guardians who always fed by the baby rather

than by the clock After a few days or a few weeks, in most cases, the baby can be led — not forced — to accept a schedule more in accordance with that which his parents would like to follow

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MASSACHUSETTS MEDICAL SOCIETY

DEATHS

HUBER — Edward G Huber, M.D., of Wahan, died July 23 He was in his sixty-fifth year

Dr Huber was born in Menomonie, Wisconsin graduated from the University of Michigan in 1903 and received his medical degree from its medical school in 1905 After a short period of private practice in Missouri, he entered the Army Medical School, graduating in 1908 Following service in the Philippines, he was sent to France during World War I and was in command of a hospital center While assigned to the First Corps Area, he attended and graduated from the Harvard School of Public Health in 1923 He retired from the Army in 1935 with the rank of colonel, and then accepted a position in the Massachusetts Department of Public Health, as well as an instructorship in the Harvard School of Public Health He was appointed acting dean of the latter in 1942 and was made associate dean and professor of public health at the time of the recent organization of the school, in which he took an extremely active part He was a member of the American College of Physicians and a fellow of the American Medical Association

His widow and a daughter survive

KINNEY — William D Kinney, M.D., of Osterville, died July 12 He was in his seventy-fourth year

Dr Kinney received his degree from Bowdoin Medical School in 1899 and had practiced in Osterville for nearly half a century He had been associate medical examiner of Barnstable County for twenty years and had always been active in the affairs of the Massachusetts Medical Society, having been a member of the Council and a supervising censor for many years, as well as president of his district society from 1913 to 1915

His widow and a son survive

STACEY — Charles F Stacey, M.D., of Blue Hill, Maine (formerly of Boston), died July 18 He was in his eightieth year

Dr Stacey received his degree from Harvard Medical School in 1892 He was a member of the Massachusetts Medical Society and a fellow of the American Medical Association

His widow survives

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

CLAGGETT — Fred P Claggett, M.D., of Newport, died July 4 He was in his seventy-eighth year

Dr Claggett received his degree from Dartmouth Medical School in 1897 He was a former president of the Sullivan County Medical Society and a fellow of the American Medical Association

A son and two daughters survive

MEDICOLEGAL ABSTRACT

Relation of Patient and Physician Liability for malpractice. A recent decision of the Supreme Judicial Court of Massachusetts contains several points of interest to the medical profession The action concerned a claim for so negligently treating a throat ailment as to cause the plaintiff's intestate to die

On November 24, 1941, the intestate was suffering from a severe cold Two days later he complained of a sore throat He did not respond to tablets and a gargle prescribed by a physician other than the defendant On November 27 he was admitted to a hospital conducted by the defendant On November 28 the patient's wife, who had worked as a practical nurse for ten years, saw him, he was very ill and cold, complained of pain in his sides, and was coughing On November 29, when his wife again saw him, his face was flushed and he was coughing up brownish sputum She told the floor nurse that he had pneumonia In stating the case the court said

If a person has a cough, a previous history of a cold and a pain in his sides, and complains of being cold, the defendant would be suspicious that pneumonia had started, and if on the next day he discovered a definite dullness on percussion of the chest, an increase in the voice sounds, bronchial or harsh breathing sounds, a flushing of the face, a high temperature and the common symptom of a rusty colored sputum containing dark-brown blood, a definite diagnosis of pneumonia could then be made A hospital record, in the handwriting of the defendant, stated that the lungs of the intestate were clear on November 27, 1941, and on November 30, 1941 According to this record, the intestate on November 30, 1941, was objecting rather violently to treatment and to taking nourishment The defendant called upon the welfare authorities to remove the intestate from the hospital On the afternoon of November 30, 1941, he was driven in an automobile by a police officer sixty to seventy miles to the Tewksbury State Hospital An examination at this hospital on the morning of December 1, 1941, disclosed that there was "bronchovesicular breathing at the left base with coarse rales throughout" The examining physician suspected that the intestate had pneumonia The intestate died on the evening of December 1, 1941

It was undisputed that the intestate was suffering from Vincent's angina when he was admitted to the defendant's hospital This disease starts with a laceration of the pharynx in the region of the tonsils, and as it progresses involves the entire mucous coating of the mouth The temperature and pulse are increased and the patient becomes very ill There may be chills and the sputum becomes rusty colored

The defendant apparently admitted that it would be improper practice for an X—— doctor to remove a patient from X—— to Tewksbury knowing that he had pneumonia, since such removal might use up his strength and cause his death An expert testified that if a patient had Vincent's angina and if it was known that he also had pneumonia, it was bad medical practice for the defendant to order his removal from X—— to Tewksbury The court was of the opinion that the question was proper, because there was evidence that the defendant should have known that the intestate had

pneumonia Where this evidence came from is not clear from the opinion.

After the expert testified as above, further examination revealed that he was not familiar with X—— practice Subsequently he was asked whether it was proper practice for a physician in a town the size of X—— to permit a man with a temperature of 100°F to be moved some sixty miles Although the layman might suppose that any well qualified doctor could answer such a question, it has long been an established rule of law that the standard of care required of a doctor depends on the standards of the particular community in which he practices, and since the witness admitted lack of knowledge concerning X—— practice, the trial judge could not properly allow him to answer this question when it was objected to by the defense

The jury found for the plaintiff, and the court was of the opinion that the evidence was sufficient to warrant such a finding

The plaintiff's declaration was for death caused by the negligent treatment of a sore throat. The evidence was such that the jury could believe that death was caused by the improper removal of the intestate from X—— to Tewksbury Ordinarily a physician may discontinue treatment of a patient without incurring liability, if his treatment, up to the time of discontinuance, has been proper In this case the physician was liable because the manner in which he discontinued the treatment was in itself the cause of injury to the patient — 1946 Adv Sh 945, July 8, 1946

CORRESPONDENCE

CHIGGERS IN MASSACHUSETTS

To the Editor This brief report I believe is justified, since it has generally been assumed that New England is free from chigger, the six-legged larva of the mite *Trombicula alfreddugesi*, otherwise known as harvest mite or red bug

I recently saw a family of four who had always lived in the heart of New York City but who had lately bought an abandoned estate in Plymouth They all had had cases of poison ivy, but they also presented a rash, especially on the legs, which to my mind was typical of chigger infestation, since I had had a chance one summer to see a large number of cases in North Carolina and Tennessee As it was night, it was impossible to look for the causative insect, but the following morning the family captured some and sent them to me, preserved in toilet water There was no question whatever about their identity, but to be absolutely sure, I sent them to Dr Howard J Parkhurst, of Toledo, Ohio, who is unquestionably this country's expert on chigger He kindly identified them for me

There also appears to be a focus of infestation in Hyannis, although I have so far been unable to capture any of the insects

Chigger infestation is of common occurrence throughout the South and up through the central states to the Great Lakes, but it has been supposed to stop in its northeastward distribution somewhere in Pennsylvania and New Jersey

AUSTIN W CHEEVER, M D

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GRADUATES OF NONAPPROVED MEDICAL SCHOOLS

To the Editor In concurring with Dr John D Lane's letter in the June 13 issue of the *Journal*, I should like to take this opportunity to elaborate further on the subject of discrimination against medical graduates of nonapproved schools

The majority of these men who have knowingly attended unapproved schools did so because they really felt the "call" to medicine There was no family desire for a doctor nor the glory of being called a "doctor" The love for the profession of their calling and their desire to help their fellow man drove them on to acquire the necessary knowledge This drive had to be very strong in order to overcome the obstacles thrown in their path by the American Medical Association's rules and regulations As a result they received more out of their education in medicine because they had to put more into it to compete with graduates of approved schools

Many graduates of unapproved schools entered the various branches of the armed forces during the past emergency as medical officers, and in every way competed on equal footing with other medical officers They were equally exposed to the same dangers, hardships, injuries and death as medical officers of approved schools and in many instances were decorated for bravery for extraordinary performance of duty Therefore it came as a great surprise to the writer that on inquiring from the Department of Medicine and Surgery of the Veterans Administration he was informed that even though graduates of unapproved medical schools are considered veterans, and were considered to have the necessary education and ability to treat the boys during the war and on the battlefields, now they are not considered capable of being assigned as residents in the veterans' hospitals In other words, the American Medical Association and its by-products, namely the specialty boards, will not permit graduates of unapproved schools who served as medical officers in one of the branches of the armed forces to be appointed as residents They have by this means prevented these men from further learning and training, which would allow them to treat their fellow man with the best possible knowledge and methods available

I have repeatedly sent letters to the Department of Medicine and Surgery of the Veterans Administration on this point, and they pass the buck on to the specialty boards — in my case the American Board of Surgery In corresponding with the secretary of this board my question "whether or not a veterans' hospital would lose its residency status if it appointed veterans of World War II who are graduates of an unapproved school as residents" is repeatedly and completely ignored Therefore, it appears to me that if the Veterans Administration is passing the buck, and in so doing preventing graduates of unapproved schools from keeping up with new methods and treatments in their field of endeavor, it is showing once again the obstacles put before these men by the mighty powers of the American Medical Association

It should also be called to the attention of those in power that the restrictions of hospital privileges and the right to practice their profession in whatever state they so desire are a definite form of discrimination These privileges should be allowed to all graduates of legally chartered medical schools who have passed the examinations given to graduates of approved schools and who have served an approved internship The refusal of allowing these privileges is fully as undemocratic as under a dictatorship The rules of the various state medical examining boards are closely regulated and governed by the American Medical Association

I should like to close with the final statement, which I believe hits the nail on the head "A school never made a man — a man makes a school"

MONROE E SHACK

Senior assistant surgeon, U S P H S (R)

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BOOK REVIEWS

Your Hair and Its Care By Oscar L. Levin, M.D., and Howard T. Behrman, M.D. 12^o, cloth, 184 pp. New York: Emerson Books, Incorporated, 1945. \$2.00.

This book, written for the lay reader, does not contain too much scientific material. The style is clear and concise, and the advice contained is quite sensible. It is a book that can be read with profit and enjoyment by both physician and patient. The final chapter, entitled "Questions and Answers," gives an excellent condensed summary of recent scientific knowledge concerning the anatomy, physiology, pathology and proper care of the scalp.

Bone-Grafting in the Treatment of Fractures By J. R. Armstrong, M.D., M.Ch., F.R.C.S. With a foreword by R. Watson-Jones, B.Sc., M.Ch. Orth., F.R.C.S. 8^o, cloth, 175 pp., with 204 illustrations. Baltimore: Williams and Wilkins Company, 1945. \$7.00.

This well written and effectively illustrated book should find a ready welcome among those who treat a large number of fractures. Methods of bone grafting are described for fractures of the spine and of the upper and lower extremity; the author usually prefers an onlay graft obtained from the tibia, which is fixed in place with nonoxidizing metal screws. Prolonged immobilization in plaster accompanied and followed by reconditioning exercises is advocated. For these procedures the no-touch technic is practiced. For the most part the author follows the usual indications for operative treatment of fractures, but in his enthusiasm he advocates its use much earlier in many cases than would be considered wise in American clinics.

A foreword by Sir Reginald Watson-Jones gives a timely warning concerning infection. Although bone grafting as the author describes it is a most valuable aid in the treatment of a number of difficult fractures, it is a matter not to be undertaken lightly, for infection is worse than nonunion or malalignment.

Penicillin and Other Antibiotic Agents By Wallace E. Herrell, M.D., M.S. 8^o, cloth, 348 pp., with 45 illustrations and 45 tables. Philadelphia: W. B. Saunders Company, 1945. \$5.00.

Publications of the Mayo Clinic bear unmistakable hallmarks: almost invariably they are well printed and clearly illustrated, are written in simple, understandable style, include a good bibliography, and are accurately and comprehensively indexed. This volume is typical of such publications.

The subject matter is divided into four parts of approximately the same length. The first part gives an admirable account of the development of penicillin, describes its method of preparation, its physical and chemical properties, how it behaves in contact with bacteria, how it is standardized, and how its concentration in body fluids can best be measured. The second and third parts are clinical. The reader unfamiliar with penicillin will find these pages of particular interest. The conditions in which the use of penicillin is indicated are well described, as is its proper method of administration and dosage. The illustrations help to make the text more interesting and more easily understood. The fourth part discusses other antibiotic agents—tyrothricin, streptothricin, streptomycin and similar substances—and brings out the far-reaching developments in medical research that the work of Dubos with gramicidin and of Fleming with penicillin has already stimulated.

Not many years ago the science of pharmacology appeared to be sluggish; chemotherapy and the discovery of antibiotics have opened an entirely new chapter in medical history, which is being studied with astonishing diligence. This book tells the whole story in an engaging fashion. It is a readable, informative and useful contribution.

NOTICES

ANNOUNCEMENT

Dr. Virgil G. Casten, having returned from over five years of naval service, has resumed the practice of ophthalmology at 412 Beacon Street, Boston.

AMERICAN DIABETES ASSOCIATION

The American Diabetes Association will hold its sixth annual session on September 16 to 18, 1946 in Toronto, Canada. The first day of the meeting will be devoted to celebrating the twenty-fifth anniversary of the discovery of insulin. The program has been arranged by the University of Toronto and will feature distinguished guests from government and medical circles. Among the latter will be Drs. C. H. Best and W. R. Campbell from Canada, Drs. E. P. Joslin, R. M. Wilder, Seale Harris, David P. Barr, and Eugene Op from the United States, Dr. R. D. Lawrence from England, Dr. H. C. Hagedorn from Denmark and Dr. B. A. Housay from Argentina. On the second day, the program has as its theme a review of the accomplishments of the past twenty-five years in various aspects of diabetes. Papers will be presented on diet, insulin, coma, gangrene, pregnancy and longevity. The third day will be divided into two sessions. The morning will consist of a presentation of experimental work and research in various phases of insulin and diabetes. The afternoon session will feature a series of short papers on recent investigations in the complications of diabetes. This will be followed by an open forum presided over by Dr. R. M. Wilder, incoming president of the American Diabetes Association. There will be a board of experts who will answer questions from the floor, in a "Stump the Experts" quiz program.

This elaborate program promises to be a fitting tribute to the memory of Dr. Frederick Banting.

CONGRESS ON INDUSTRIAL HEALTH

The schedule of events for the seventh annual Congress on Industrial Health, which is to be held at the Copley-Plaza Hotel, Boston, September 30 through October 2, is as follows:

Monday, September 30

Clinical Toxicological Conference	All day
Topic — "Lead Poisoning"	
Surgical Conference	
Topic — "The Foot in Industry"	Afternoon
Professional Relations Conference and Dinner	Evening

Tuesday, October 1

General Session	Morning
Topic — "Human Relations in Industry"	
Elective Seminars	Afternoon
Section A — Industrial Physiology	
Section B — Administrative Methods	
Section C — Workmen's Compensation	
Dinner and Conference on Pan-American Industrial Health	Evening

Wednesday, October 2

General Session	Morning
Topic — "Atomic Energy: Its effects in industry and medicine"	Afternoon
General Session	Afternoon
Topic — "A Positive Health Program for Industry"	
Dinner and Conference on Health and Welfare Programs in Industry	Evening

NEW ENGLAND HOSPITAL
FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, September 5, in the classroom of the Nurses' Residence at 7:15 p.m. Dr. Felicia A. Banas will discuss mesenteric thrombosis, and Dr. Wyland F. Leadbetter, genitourinary tuberculosis. Dr. Grace E. Rochford will be chairman.

(Notices continued on page xvii)

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THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS WITH PENICILLIN IN PEANUT OIL AND BEESWAX*

ARTHUR J. GEIGER, M.D.,† AND JESSAMINE R. GOERNER, M.D.‡

NEW HAVEN, CONNECTICUT

THE apparent curability of subacute bacterial endocarditis with penicillin has been unequivocally established within the last two years.¹ The essentials of successful therapeutics consist of treatment with massive daily doses of penicillin for a month or longer, the actual amount given daily depending on the resistance of the infecting organism to penicillin and on the serum penicillin concentrations attained. Supplementation of the penicillin with heparin, as first advocated by Loewe and his associates,² has proved unnecessary in our experience³ as well as that of others,¹ and the dispensability of this costly and usually troublesome adjuvant has gratifyingly simplified the therapeutic regimen. The necessity for prolonged and uninterrupted parenteral treatment in this disease, however, has imposed a considerable task on the professional attendants and has demanded no small measure of fortitude from the patients, who must either submit to intramuscular injections at hourly or two-hourly intervals night and day or tolerate continuous intravenous or intramuscular infusion for weeks and sometimes for months. These difficulties and objections could be largely eliminated if satisfactory and sustained serum penicillin levels were attainable, either with oral medication or by the infrequent injection of massive deposits of penicillin in a slowly absorbable form.

ORAL ADMINISTRATION OF PENICILLIN

The considerable destruction of penicillin in the stomach and the ready absorbability of certain drugs from the sublingual mucous membrane led to a preliminary trial of penicillin by this route in 3 patients. Penicillin was administered in small triturated tablets in 50,000-unit amounts, but no penicillin was detected in blood samples taken at half-hour intervals during the next five hours.

The ingestion of penicillin tablets, solutions or suspensions, with or without antacid buffering and

adsorbing agents, is already well known to yield appreciable amounts of penicillin in the blood.⁴ For the treatment of subacute bacterial endocarditis, however, this form of medication cannot yet be considered feasible — first because oral doses must be at least several times as large as parenteral doses to achieve comparable serum concentrations, which makes the cost of prolonged treatment prohibitively high, and second because it is necessary to repeat oral medication at about two-hour intervals night and day to maintain effective serum concentrations, and this is obviously objectionable when treatment must be carried on for weeks and months. For these reasons the treatment of subacute bacterial endocarditis with penicillin given orally has not been considered feasible thus far.

PARENTERAL DEPOSITS OF PENICILLIN IN SLOWLY ABSORBABLE FORM

Romansky⁵ has recently developed a slowly absorbable preparation of penicillin for parenteral use by suspending the drug in a mixture of peanut oil and beeswax, and he has demonstrated that ample and prolonged concentrations of penicillin in the blood serum follow single injections of 1 cc. or more of a mixture containing 300,000 units per cubic centimeter.⁶ Moreover, the therapeutic efficacy of this preparation in the cure of large numbers of cases of gonorrhea and syphilis given one injection daily has already been conclusively established.^{7, 8}

During the past year we had a unique opportunity to compare the effect of penicillin in oil and beeswax with that of water-soluble penicillin in the treatment of a patient with subacute bacterial endocarditis who, although refractory to cure, could be kept asymptomatic, afebrile and with sterile blood cultures so long as he received at least 250,000 units of penicillin parenterally each day, either in two-hourly intramuscular injections or by continuous intravenous drip. If a similar therapeutic remission could be maintained indefinitely with a single daily injection of penicillin in oil and beeswax, continued hospitalization would no longer be necessary, and

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the patient might be able to survive without symptoms and with no more restriction or inconvenience than that imposed on a diabetic patient taking insulin. This result was achieved in the case that follows.

CASE 1 V. H., a 45-year-old engineer, in June, 1944, developed symptoms and signs of subacute bacterial endocarditis on a background of rheumatic heart disease with mitral and aortic valvular lesions. The infecting organism, *Streptococcus viridans*, proved inhibitable in vitro by penicillin concentrations of 0.04 units per cubic centimeter of culture. Treatment for 10 months with water-soluble penicillin in daily doses ranging from 240,000 to 600,000 units and administered either in fractionated intramuscular injections

been interrupted for 3 weeks, an Osler's node appeared on one finger, without other developments except bacteremia.

The demonstration in this case that single daily injections of penicillin in oil and beeswax could maintain clinical remission and sterility of the blood just as effectively as had been previously accomplished with parenterally administered water-soluble penicillin encouraged us to try this form of therapy in the next case.

CASE 2 A. B., a 59-year-old housewife, had been ill for 5 months with fatigue, anorexia, periodic fever and night sweats. During this period she lost 35 pounds in weight. The

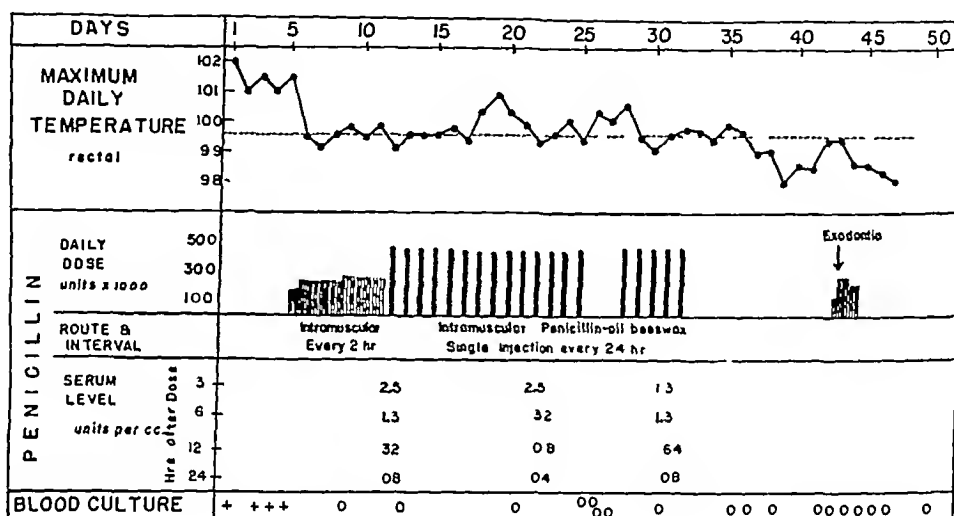


FIGURE 1 Case 2

at two-hour intervals or by continuous intravenous drip was regularly attended by clinical remission and sterilization of the blood. Whenever treatment was interrupted to evaluate the clinical status, however, *Str. viridans* promptly reappeared in the blood. The extraction of an infected tooth and removal of the spleen, which were suspected as foci of reinfection, did not alter the course. The infecting organism did not change its resistance to penicillin in vitro during this long period. Although this 10-month treatment failed to cure the patient, it was apparent that he could be kept clinically well and with sterile blood so long as penicillin was regularly furnished.

Following a few test injections of penicillin in oil and beeswax in June, 1945, sustained treatment with this preparation* was begun in July and was continued until December 14. The injections, which were given intramuscularly, consisted of 300,000 to 450,000 units of penicillin, given either once daily or on alternate days in doses of 600,000 units. Treatment was periodically interrupted for brief intervals to evaluate the clinical status.

During the periods of daily treatment the patient remained afebrile and clinically asymptomatic, and the blood cultures were consistently sterile. The 600,000-unit doses at two-day intervals were abandoned after a month's trial because bacteremia was not consistently suppressed by this regimen. The patient gained several pounds in weight, gradually resumed an approximately normal level of activity and received permission to return to his work during the fall. That he was not cured, however, was apparent from the regular return of bacteremia within 2 weeks of any interruption in therapy. The patient kept a daily chart of his afternoon temperature for 6 months after his discharge, and throughout this period he remained afebrile. On one occasion, when treatment had

past history included erythema nodosum in 1938, acute appendicitis in 1942 and typhoid fever at the age of 6, when, the patient asserted, a heart murmur was noted.

Physical examination disclosed an appearance of chronic illness but no wasting of the body. The heart, which was moderately enlarged, presented a harsh and moderately loud systolic murmur over the entire precordium, together with a faint systolic thrill at the apex. The liver edge was barely palpable, but the spleen was not felt. The finger ends were slightly club-shaped, and a fading petechia was noted over the left malleolus. There was a moderate hypochromic anemia with a white-cell count of 15,000 cells, 85 per cent of which were neutrophils. The blood was negative serologically, the urine was normal, and an electrocardiogram was normal. Roentgenograms of the chest showed moderate enlargement of the left auricle and ventricle. Four cultures of the blood revealed *Str. viridans* (two colonies per cubic centimeter) and the organism proved inhibitable by 0.02 units of penicillin per cubic centimeter of culture.

During the first 5 days, the rectal temperature reached 101 and 102°F, but within 24 hours of the commencement of penicillin therapy it fell below 100°F, and it remained there through most of the ensuing 6 weeks in the hospital. Following the preliminary administration of regular penicillin in doses of 20,000 units intramuscularly at 2-hour intervals for 6 days, treatment was changed to a single daily intramuscular deposit of 1.5 cc. (450,000 units) of penicillin in oil and beeswax, and the injections were continued for 19 days longer. Cultures of the blood continued sterile throughout the period of treatment no petechiae appeared, and the appetite and strength soon returned. At about the midpoint of the penicillin course, slight clouding of vision on the right developed accompanied by slight edema in the region of the macula and continued for several days. Shortly before discharge an unruptured and a devitalized tooth were extracted, and penicil-

*The material was supplied for experimental use in this case through the courtesy of Dr. Charles Church of E. R. Squibb & Sons, New York City.

lin and sulfadiazine were given prophylactically for 2 days following the operation. The clinical course and laboratory data are illustrated in Figure 1. One week after discharge, generalized urticaria developed for several days.

Since termination of the formal course of treatment on November 16, 1945, the patient has continued entirely well and without congestive failure. She has gained 16 pounds in weight, and all of fifteen blood cultures have been sterile.

The apparently successful outcome in this patient treated almost entirely with penicillin in oil and beeswax led us to treat the next case with this preparation alone.

CASE 3. M W, a 40-year-old housewife, had had rheumatic fever at the age of 20 and was known to have had a heart murmur since then. In December, 1945, she developed insidious fever, drenching sweats and amenorrhea and lost 7 pounds in weight. Her physician noted several petechiae in the 2nd week of illness, and a blood culture made at that time yielded *Str. viridans*. Treatment with penicillin was begun promptly at another hospital, and the patient received 210,000 units daily for 25 days intramuscularly, in doses of 35,000 units every 4 or 5 hours. Although fever and symptoms subsided during the period of treatment, the patient relapsed both clinically and bacteriologically within a week of the termination of therapy. She entered the New Haven Hospital for further treatment on February 18, 1946.

The abnormal findings on admission included a temperature of 102.6°F, an Osler's node on a fingertip, two subungual hemorrhages and a petechia on an eyelid and another on the right breast. The spleen was barely palpable. The heart, which was moderately enlarged, presented a loud, harsh and long apical systolic murmur with wide transmission. The heart sounds were otherwise normal, and there was no congestive failure.

A moderate anemia without leukocytosis was present. Four successive blood cultures were positive for *Str. viridans* (10 colonies per cubic centimeter), and the organism proved inhibitable by 0.02 units of penicillin per cubic centimeter in vitro.

Treatment consisted entirely of intramuscular deposits of penicillin in oil and beeswax. Because a single injection of 1 cc (300,000 units) was found to yield serum penicillin concentrations of 0.16 units per cubic centimeter at the end of 12 hours and less than 0.04 units at the end of 24 hours, it was decided to repeat the doses at 12-hour intervals, and this was done for 30 days. Symptoms subsided within a week, no further petechiae appeared, the spleen became impalpable, and the patient gained 4 pounds in weight. Cultures of the blood were sterile throughout the period of treatment and also during a deliberate interruption of therapy for 48 hours near the end of the therapeutic course. A moderate elevation of the erythrocytic sedimentation rate and an irregular fever of about 1°F, which persisted throughout the period of treatment, was attributed to the penicillin in oil and wax, for each deposit caused considerable local pain and some swelling, with occasional local redness. The temperature became normal within 48 hours of the cessation of the injections and remained so.

The treatment was stopped on March 25. The patient has remained asymptomatic and has resumed her household activities, and nine successive cultures of the blood have been sterile. She has gained another 4 pounds in weight, and the amenorrhea, which was present for 4 months, has given way to normal menstruation.

SERUM PENICILLIN CONCENTRATIONS

Intramuscular deposition of various amounts of the penicillin in oil and beeswax mixture in 5 patients yielded serum penicillin concentrations through forty-eight-hour periods, as shown in Table 1. Reasonably adequate levels were usually noted for twelve hours, and appreciable amounts of penicillin were often still present at the end of twenty-four hours. The fairly wide scattering of values at any time interval following an injection

suggests either considerable variation in the relative rates of absorption and excretion of the penicillin or deficient potency of some of the doses. Most of the material had been supplied in 10-cc vials, and it is conceivable that the reheating of such vials for

TABLE 1 Serum Penicillin Concentrations

DOSE units	HOURS FOLLOWING INJECTION						
	1	3	6	9	12	24	48
	units/cc	units/cc	units/cc	units/cc	units/cc	units/cc	units/cc
300 000	0.64* 0.03	0.64 0.03	0.64 0.03	1.28† 0.04	0.32 0.16 0.16 0.03 0.04	0.03† 0.04 0.02 0.04 0.04	0.04 0.04 0.04 0.04 0.04
450 000		2.5 2.5 1.28	1.28 1.28 0.32	0.03	0.64 0.32 0.03	0.03 0.03 0.04	0.03 0.03 0.03
600 000				0.64 0.64		0.03 0.03	0.04 0

*The italicized figures refer to Case 1.

†In a 3 year-old child.

injections of 1 cc may have reduced potency. On the other hand, from his much larger experience, the material is relatively heat-stable.

DISCUSSION

In the absence of previous reports of patients receiving penicillin in oil and beeswax for several weeks to months, observations regarding local and general untoward effects from such injections are of interest. The patient in Case 1 suffered only minimal local discomfort from the daily injections, practically all of which were given into the lateral aspects of the thighs. Slight local swelling was sometimes apparent for a few days, but even after six months of almost daily deposits there was no apparent local induration or lumpiness. It is also of interest that although this patient had a history of hay fever with occasional mild asthma, no allergic manifestations, either local or general, made their appearance in spite of several interruptions of the therapeutic course. The patients in Cases 2 and 3 suffered considerable local swelling and soreness, sometimes with erythema, which lasted for several days following each injection. The buttocks proved definitely preferable to other sites for the injections in these cases. In Case 2, a week following the last injection profuse urticaria developed for the first time in the patient's life. Five months later skin patch and scratch tests with penicillin, peanut oil and the penicillin-oil-wax mixture were performed, with negative results. Two slightly tender subcutaneous nodules, probably attributable to the previous therapy, were noted in the buttocks at that time.

In the beginning the handling and injection of the semisolid mixture proved extremely troublesome and difficult. Observance of the following technical details eliminated all difficulties. The ampule of material was kept at room temperature for a few

hours before use — it may be stored at room temperature — and was heated in water at 45°C for several minutes to melt the material and render it injectable. The needles and syringe, which must be scrupulously dry, were also warmed to prevent cooling and congealing of the material during the injection. The warmed mixture, when flowing freely in the tilted vial, was quickly withdrawn through a 15-gauge needle into a 2-cc or 3-cc syringe with a snugly fitting piston, the air seal could be improved by applying a drop of sterile mineral oil to the distal half of the piston. The injection was made without delay through a 20-gauge needle. Lastly, more effective injection force was applied by the use of a syringe whose barrel was equipped with a pair of finger grippers.*

The attainability of considerable concentrations of penicillin in the serum for prolonged periods following single injections of penicillin in a mixture with oil and beeswax and the demonstration of the apparent curability of subacute bacterial endocarditis with this preparation given once or twice daily for several weeks offer a therapeutic regimen far simpler for both the patient and the professional attendants than any previously employed in the treatment of this disease. The question naturally arises whether, with this form of penicillin, patients may be treated at home and spared the long and costly hospitalization hitherto required. This would admittedly be feasible provided certain minimum bacteriologic controls were not neglected. The infecting organism in every case should be isolated from the blood, identified as a species reasonably inhibitable by penicillin and tested for its sensitivity to penicillin. Finally, one should have assurance that the concentrations of penicillin attained in the blood under the conditions of the treatment generously exceed the minimal inhibition level of the organism. To treat without such bacteriologic controls is to invite defeat through either inadequate dosage or too long intervals between injections — circumstances that may occasionally lead to increased resistance of the infecting organism to penicillin. Under circumstances in which bacteriologic facilities are minimal, some measures of control of the therapy may be achieved by the following simple and abbreviated procedure. One cubic centimeter of the patient's serum, previously warmed to 56°C for five minutes to eliminate serum-inhibiting factors,⁹ is diluted with three volumes of broth media and is inoculated with an eighteen-hour blood-broth culture of the patient's organism, a tube containing 4 cc of broth only is similarly inoculated as a control for viability of the organism. Inhibition of growth in the tube containing serum implies that the penicillin concentrations are at least four times as high as the inhibition level of the organism concerned. Preliminary experiments for comparing this technic with actual measurements of the penicillin

serum levels, with a minor modification of the method of Rammelkamp,¹⁰ suggest that it is valid.

Two favorable factors probably contributed to the rapid apparent cure in 2 of our cases. In the first place, the infecting organisms proved relatively sensitive to penicillin *in vitro*. In the second place, satisfactory concentrations of penicillin were attained in the blood with either a single daily injection of 1.5 cc or a twice-daily injection of 1 cc. The coincidence of such favorable circumstances cannot be taken for granted. Recent reports of extensive studies in patients treated for venereal diseases indicate that injections of 1 cc (300,000 units) fail to maintain serum penicillin concentrations in excess of 0.10 unit for more than twelve hours in the majority of cases, and that more voluminous injections serve chiefly to raise the initial serum levels rather than to prolong the effects.^{7, 8} One may infer from this that most cases of subacute bacterial endocarditis require injections at twelve-hour intervals to assure maintenance of serum penicillin levels high enough to inhibit the majority of strains of *Streptococcus viridans*.

SUMMARY

Apparent cure in 2 cases of subacute bacterial endocarditis due to *Streptococcus viridans* was effected with one or two daily injections of massive doses of penicillin in a mixture of peanut oil and beeswax.

In another case, which had proved refractory to cure after ten months' treatment with water-soluble penicillin given parenterally, an afebrile and asymptomatic state with sterility of the blood was maintained with a single daily injection of penicillin in oil and beeswax. Positive blood cultures, however, were obtained whenever this treatment was discontinued. It is believed that this patient can be kept indefinitely in a state of remission by this simple ambulatory form of treatment.

Satisfactory serum-penicillin concentrations were present for twelve hours and often for twenty-four hours following a single injection of 300,000 to 600,000 units of penicillin in oil and beeswax.

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*Becton-Dickinson syringe (No. LC 3) was found highly satisfactory.

STATISTICS OF DIABETES*

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THE statistics of diabetes will be considered under eight headings — prevalence of diabetes, characteristics of the diabetic population, mortality from diabetes, international comparisons, trend of diabetes in wartime, significance of geographical variations in diabetes, longevity of diabetic patients and use of statistics in clinical diabetes

PREVALENCE OF DIABETES

The first consideration is the total volume of diabetes in the country. Frankly, it is not known with any degree of accuracy how many diabetic persons there are in the United States, but there is a certain body of facts on which to work. Some guidance can be gained from the annual death toll. In 1943, the last year for which statistics for the entire country are available, the number of deaths recorded as due to diabetes within the country was 36,314. At that time, there were approximately 2,500,000 Americans serving abroad in the armed forces, but the number of deaths from diabetes among them — the pick of the young men — was negligible. During the last five years, the number of deaths from diabetes has averaged nearly 35,000 per annum.

Not all deaths of diabetic persons are recorded as due to diabetes. There is a certain degree of understatement arising out of the fact that deaths of diabetic patients from such causes as cancer, tuberculosis and accidents are classified under these other causes. Thus, in 1940 in the United States, 3991 deaths were reported in which diabetes was secondary to some other cause, as compared with 35,015 in which it was the primary cause of death. The total number of persons reported as dying *with* diabetes, 39,006, was 11 per cent greater than the number recorded as dying from diabetes. In other cases, the diabetes has not been mentioned on the death certificate because the physician certifying the death did not consider that the diabetes caused it or because he did not know that the patient was diabetic. The study of Joslin and Lombard¹ indicates that the total number of deaths from diabetes may be understated by as much as 50 per cent. If one is conservative and assumes an understatement of 25 per cent, this means that the number of persons dying annually *with* diabetes is of the order of 45,000.

A rough approximation of the total number of diabetic persons may be made from the total number of deaths, together with such facts as are at

hand on the longevity of these persons. The latest figures from the George F. Baker Clinic give the average duration of diabetes from onset to death as twelve years. Crude estimates based on life-table analyses of the mortality among patients of the clinic yield a somewhat higher figure — between fifteen and twenty years. These figures, however, are probably significantly higher than would be found true for the population as a whole. For example, a study in Philadelphia² showed a duration of only seven and five-tenths years. There are probably no more than 15 living diabetic persons per diabetic death. Applied to the reported number of deaths from diabetes, this would yield a figure of 525,000, applied to the estimate of persons dying *with* diabetes, it would yield one of 675,000.

The other sources of information on the number of diabetic persons are various surveys of the population. Three such sources will be discussed — the National Health Survey of 1935–1936 and the studies among selectees in Boston and in New Orleans.

The National Health Survey, conducted during the winter of 1935–1936 under the auspices of the United States Public Health Service, covered approximately 2,500,000 persons living in seven hundred thousand households in eighty-three cities. It was so planned as to constitute a representative sample of the general urban population of the country. Some rural families were canvassed but were excluded in the final analysis of data. The facts on disease as reported by members of households were recorded by trained enumerators. Wherever possible, an effort was made to confirm these statements through attending physicians. Among the families surveyed, 9182 cases of diabetes were reported, a total equivalent to 3.5 per 1000 population.³ When the rates by sex and age were applied to the country as a whole as of the date of the survey, the resulting estimate of diabetic persons in the country was 450,000. Certain further adjustments of the figures, however, were made by the statisticians of the Public Health Service. The report of the National Health Survey contained an estimate of 660,000 diabetic persons in the country as of 1937.⁴ Applying the prevalence rates by sex and age to the 1940 population yields a total of 500,000 diabetic persons in that year, and if the same adjustment were applied to this figure as was done in the 1937 estimate, the total in 1940 would be 725,000.

With regard to the National Health Survey, there are certain points to be emphasized. First, the survey estimate was based on the urban population covered. As will be seen, available statistics show

*From the Statistical Bureau, Metropolitan Life Insurance Company. A lecture given in the Postgraduate Course on Diabetes, Harvard Medical School, October 1, 1945.

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that, age being considered, the prevalence of diabetes is higher in the city than in the country. Hence, on these grounds, estimates for the country as a whole, based on the National Health Survey, would tend to be high. On the other hand, a survey such as this could not be expected to identify every case, a deficiency that is offset only in part by errors of the opposite kind — namely, the inclusion of persons reported as diabetic who were not so. It is not known which of the two factors — the use of urban data in the estimate or the unavoidable failure to include some cases in the survey — is of the greater importance. Apart from this, the method and extent of the adjustment of the basic figures of the survey that yielded the 1937 estimate of 660,000 are of doubtful validity. All in all, however, the basic unadjusted figures of the National Health Survey may be considered minimal.

Data based on Selective Service findings such as were reported by Blotner, Hyde and Kingsley⁵ are significant in that such studies cover a relatively but not wholly unselected group of males within a certain age limit. Blotner and Hyde's figures for the Boston area are extraordinarily high — so high, in fact, that for reasons that have been published elsewhere,⁶ one must be cautious about accepting them at face value. Thus, the prevalence rates in this sample, analyzed by age, were three to five times as high as in the National Health Survey. It is notable, moreover, that the number of previously known diabetic persons in the group was approximately what would be expected on the basis of the National Health Survey prevalence rates at these ages. These previously known cases constituted only one fifth of the diabetic total. Fortunately, efforts are under way to collect similar data elsewhere and to follow up the cases first diagnosed as diabetic on Selective Service examination, to see whether the diagnosis is confirmed on subsequent examination. Certainly, if the Blotner and Hyde figures are valid, this means a sharp upward revision in the estimates of the diabetic population, at least at the young adult ages.

In sharp contrast to the Boston figures are those published by Spellberg and Leff,⁷ who reported on the findings at the New Orleans Induction Station during 1944. There, among 32,000 consecutive selectees, only 37 men with glycosuria were found, and of these only 9 were diagnosed as true diabetic patients. The proportion with glycosuria was thus only 1 per 1000, as compared with 8 in Boston. The corresponding figures for diabetes were 0.3 and 4.5 per 1000, respectively. Even eliminating the older men from the Boston series, because few of the New Orleans selectees in 1944 were over thirty-five, there is still a wide gap between the two studies. Spellberg and Leff cite a number of factors that bear on the situation, but the difference is too large to be accounted for by these factors alone.

Another important point regarding estimates of prevalence of diabetes is that the diabetic population is not static, so that any set of estimates needs to be revised periodically. The population continues to increase, and at the same time there is occurring a change in its internal composition that is significant with regard to diabetes — namely, the relative increase in the population at the older ages, and more especially the female population, among whom the prevalence of diabetes is highest. Other things being equal, this brings about a more rapid increase in the diabetic population than in the general population. Still another consideration is that the increasing longevity of diabetic patients will, for some time to come, at least, widen the margin between the number of new diabetic patients discovered each year and the number of such patients dying each year. An analysis based on the prevalence figures of the National Health Survey and the mortality among diabetic patients indicates that the number of new cases of the disease is at least 50,000 a year.¹ How much higher the actual figure is, one has no way of knowing, but it may be as high as 75,000 a year. This may be matched against the figure of 35,000 deaths from diabetes and the estimate of 45,000 deaths of persons *with* diabetes. On the basis of these figures, the annual increase in the diabetic population lies somewhere between 5000 and 30,000 a year. Computations based on the prevalence rates of the National Health Survey, together with estimates of future population, indicate a net increase of 10,000 diabetic patients a year.

CHARACTERISTICS OF THE DIABETIC POPULATION

It is of interest to see how the diabetic population is constituted. The chief features of its makeup, in 1940, estimated from the prevalence rates of the National Health Survey, were as follows: 38.5 per cent of the diabetic persons were males and 61.5 per cent were females, a ratio of 10:16. In childhood and young adult life the extent and the prevalence rates of diabetes for males and females are approximately the same. Between the ages of thirty and eighty, there is a sharp sex divergence. The maximum difference in prevalence rates between the sexes is seen between forty-five and sixty-five, when the rates for females are approximately double those for males. There is some doubt whether there is any sex difference in diabetes prevalence rates in extreme old age because of the small number of observations at the later ages of life. Of course, there are many more aged diabetic women than men because at these ages women far outnumber men in the general population.

The prevalence rates in both sexes showed a steady increase with age to a maximum in the early seventies. At ages under thirty, less than 1 person per 1000 population was found to be diabetic in the

ational Health Survey In the early seventies, somewhat over 15 per cent of the male population and about 25 per cent of the female population, was found to be diabetic

MORTALITY FROM DIABETES

The latest available national data on deaths from diabetes, those for 1943, showed it to be eighth in rank among the causes of death and seventh in rank among the diseases. Among white women over forty-five years of age, diabetes was fifth in rank among the causes of death. The importance of this disease in middle-aged and older women is shown by the fact that in 1943 it caused three times as many deaths among white women older than forty-five as did tuberculosis.

The country's death rate from diabetes in 1943, based on the 36,314 deaths recorded among persons resident in the country, was 27.1 per 100,000 estimated population. This was the highest crude death rate for diabetes recorded in the United States up to the present time. It must be borne in mind, however, that the rate was artificially somewhat increased by the absence abroad of large numbers of young men and women, among whom the death rate from diabetes is particularly low, since the armed forces exclude known diabetic patients. Indications are that the crude death rate fell moderately during 1944, as well as thus far in 1945. The present year's record is comparatively favorable because of the extremely low prevalence of respiratory disease during the past winter.

The trend of the recorded death rate of diabetes in the United States has been generally upward for the entire period during which statistics of causes of death have been assembled in this country. This has held true even since insulin became available for the treatment of diabetes. The highest rates in the country's history have been recorded in recent years. Facts for the country as a whole over the years are not available. Registration of deaths in many of the states was unsatisfactory until comparatively recent years, and only since 1933 have statistics for the entire country been available. In 1900, registration was satisfactory in only ten states and the District of Columbia. These comprise what are called the "Original Registration States." Studies in long-term trends of mortality are generally best related to the findings in these states, since they differ materially from the country as a whole in the composition of their population as regards sex, race and age.

In the Original Registration States in 1900, the death rate from diabetes was 11.0 per 100,000. In 1940, the rate in the same area was 35.5, or over three times the rate in 1900. In the later year, the rate for the entire country was 26.6 per 100,000. As has been indicated, an appreciable part of the rise in the diabetes mortality is due to the increasing proportion of older persons in the population. A recent

publication of the Census Bureau³ shows that when the sex-age specific rates for earlier years are adjusted to the 1940 population, the death rate for 1900 is increased from 11.0 to 13.0 per 1000, and the increase in the diabetes rate for the Expanding Registration Area is a trifle over 100 per cent after such adjustment, as against an increase of 140 per cent in the unadjusted rate.

The effect of the change in the age composition of the population on the death rate of diabetes is further shown by the fact that the average annual increase in recorded rates between 1921 and 1940 is 1.4 per cent when allowance is made for such changes, as compared with an increase of 2.5 per cent per annum before such allowance is made.

The increase in this death rate in the last decade or so has been comparatively slight. Between 1933, when mortality data first became available for the entire country, and 1940, the death rate, adjusted to the 1940 population distribution, increased only from 24.1 to 26.6, or a trifle over 10 per cent. Statistics of the Metropolitan Life Insurance Company show that between 1931-1933 and 1941-1943 the death rate of diabetes at all ages combined, when adjusted to allow for changes in the age and sex composition of the insured population, displayed a moderate decline among white males, a very slight increase among Negro males and a slight decrease among females, both white and Negro. Similar comparisons of 1941-1943 with 1921-1923 show a moderate decline among white males but substantial increases among white females and among Negroes of both sexes. When the data are analyzed by age, however, there are found substantial decreases at every age up to fifty-five among white persons of both sexes. It is thus only among older persons that increases in diabetes death rates are found, and such increases in recent years have been relatively small. Similar data by age for the United States between 1920 and 1940, undifferentiated as regards race and sex, show sharply lowered rates among young persons. The decline extends up to the age of forty-five, whereas marked increases in the rate are closely limited to the age of sixty-five and over.

Urban death rates from diabetes, regardless of the size of the city, are considerably higher than the rates in rural areas.³ In 1940, the adjusted urban rate at all ages was over one and a half times as high as that in rural areas. In the aggregate, the rates for the cities show no marked differentials according to size of city. Such a differential does exist for females but not for males. In every group, however, the highest rate is found in the cities of 100,000 or more.

The mortality from diabetes among white persons is now little higher than that among Negroes. For both sexes combined, the white rate in 1940, adjusted for differences in the sex and age composition of the population groups, was 15 per cent above the Negro

that, age being considered, the prevalence of diabetes is higher in the city than in the country. Hence, on these grounds, estimates for the country as a whole, based on the National Health Survey, would tend to be high. On the other hand, a survey such as this could not be expected to identify every case, a deficiency that is offset only in part by errors of the opposite kind — namely, the inclusion of persons reported as diabetic who were not so. It is not known which of the two factors — the use of urban data in the estimate or the unavoidable failure to include some cases in the survey — is of the greater importance. Apart from this, the method and extent of the adjustment of the basic figures of the survey that yielded the 1937 estimate of 660,000 are of doubtful validity. All in all, however, the basic unadjusted figures of the National Health Survey may be considered minimal.

Data based on Selective Service findings such as were reported by Blotner, Hyde and Kingsley⁵ are significant in that such studies cover a relatively but not wholly unselected group of males within a certain age limit. Blotner and Hyde's figures for the Boston area are extraordinarily high — so high, in fact, that for reasons that have been published elsewhere,⁶ one must be cautious about accepting them at face value. Thus, the prevalence rates in this sample, analyzed by age, were three to five times as high as in the National Health Survey. It is notable, moreover, that the number of previously known diabetic persons in the group was approximately what would be expected on the basis of the National Health Survey prevalence rates at these ages. These previously known cases constituted only one fifth of the diabetic total. Fortunately, efforts are under way to collect similar data elsewhere and to follow up the cases first diagnosed as diabetic on Selective Service examination, to see whether the diagnosis is confirmed on subsequent examination. Certainly, if the Blotner and Hyde figures are valid, this means a sharp upward revision in the estimates of the diabetic population, at least at the young adult ages.

In sharp contrast to the Boston figures are those published by Spellberg and Leff,⁷ who reported on the findings at the New Orleans Induction Station during 1944. There, among 32,000 consecutive selectees, only 37 men with glycosuria were found, and of these only 9 were diagnosed as true diabetic patients. The proportion with glycosuria was thus only 1 per 1000, as compared with 8 in Boston. The corresponding figures for diabetes were 0.3 and 4.5 per 1000, respectively. Even eliminating the older men from the Boston series, because few of the New Orleans selectees in 1944 were over thirty-five, there is still a wide gap between the two studies. Spellberg and Leff cite a number of factors that bear on the situation, but the difference is too large to be accounted for by these factors alone.

Another important point regarding estimates of prevalence of diabetes is that the diabetic population is not static, so that any set of estimates needs to be revised periodically. The population continues to increase, and at the same time there is occurring a change in its internal composition that is significant with regard to diabetes — namely, the relative increase in the population at the older ages, and more especially the female population, among whom the prevalence of diabetes is highest. Other things being equal, this brings about a more rapid increase in the diabetic population than in the general population. Still another consideration is that the increasing longevity of diabetic patients will, for some time to come, at least, widen the margin between the number of new diabetic patients discovered each year and the number of such patients dying each year. An analysis based on the prevalence figures of the National Health Survey and the mortality among diabetic patients indicates that the number of new cases of the disease is at least 50,000 a year.¹ How much higher the actual figure is, one has no way of knowing, but it may be as high as 75,000 a year. This may be matched against the figure of 35,000 deaths from diabetes and the estimate of 45,000 deaths of persons *with* diabetes. On the basis of these figures, the annual increase in the diabetic population lies somewhere between 5000 and 30,000 a year. Computations based on the prevalence rates of the National Health Survey, together with estimates of future population, indicate a net increase of 10,000 diabetic patients a year.

CHARACTERISTICS OF THE DIABETIC POPULATION

It is of interest to see how the diabetic population is constituted. The chief features of its makeup, in 1940, estimated from the prevalence rates of the National Health Survey, were as follows: 38.5 per cent of the diabetic persons were males and 61.5 per cent were females, a ratio of 10:16. In childhood and young adult life the extent and the prevalence rates of diabetes for males and females are approximately the same. Between the ages of thirty and eighty, there is a sharp sex divergence. The maximum difference in prevalence rates between the sexes is seen between forty-five and sixty-five, when the rates for females are approximately double those for males. There is some doubt whether there is any sex difference in diabetes prevalence rates in extreme old age because of the small number of observations at the later ages of life. Of course, there are many more aged diabetic women than men because at these ages women far outnumber men in the general population.

The prevalence rates in both sexes showed a steady increase with age to a maximum in the early seventies. At ages under thirty, less than 1 person per 1000 population was found to be diabetic in the

quently reported it is least accurately reported. Search for cases of the disease will be well rewarded.

LONGEVITY OF DIABETIC PATIENTS

As against the steady increase in the diabetes death rate in the general population, there is the striking paradox that diabetic patients, particularly since the introduction of insulin, have shown steady gains in longevity¹¹ and that this has been associated with improvement in their general health and working capacity¹². The diabetic child of two generations ago could look forward to but a year or two of severely restricted life. Today, the expectation of life of the average diabetic child aged ten is estimated at forty years. Similar, though smaller, gains have been recorded among diabetic patients at other periods of life. Naturally, the gain is progressively smaller with increasing age. It is thus clear that the increase in mortality from diabetes in the general population can be explained only by a large and steady increase in the number of known diabetic patients. It is impossible in this lecture to go into the matter in detail, but the chief reasons are the increase in the proportion of older persons in the population, the more frequent discovery of diabetes as the result of improved diagnostic aids and the wider application of these measures, and certain environmental conditions that favor the onset of the disease in predisposed persons.

It is significant, furthermore, that life-table analysis of the causes of death among diabetic patients shows a reduction in the rates of death from most causes, especially those that reflect the degree of control of the diabetes.¹³ Thus, the rate of death from coma has declined progressively and rapidly. This applies likewise in a measure to tuberculosis, pneumonia and even to gangrene. The new chemotherapeutic agents promise even further reductions in many of these causes and in particular, fortunately, in diabetic gangrene. Cancer is the only important cause of death to show some increase, and this is not unexpected in view of the similar trend in the general population and the increased longevity of diabetic patients.

THE USE OF STATISTICS IN CLINICAL DIABETES

This discussion of the use of statistics in studies of diabetes is necessarily limited to certain broad considerations. Because of the rapid advances in the treatment of diabetes, and because it is a disease in which quantitative laboratory measurements are so important, there is more room and more need for statistics in clinical diabetes than in most fields of medicine. I need hardly remind this audience of the real differences of opinion that exist regarding the management of diabetes generally and of certain phases of the disease. The solution of the problems involved in these conflicting opinions can be expedited by the collection and analysis of clinical statistics by individual physicians or even by groups

of physicians following more or less the same methods. The statistical method enables the physician to substitute facts for impressions on specific matters of treatment, as well as to compare results obtained with similar findings elsewhere. When such analysis reveals significant differences, it puts the physician on the alert to ferret out the causes and to introduce such changes in methods as the facts suggest. In teaching the subject of diabetes to medical students, the statistical approach is often effective.

There is also a broad field of community service to diabetic patients in which collection and analysis of statistics is of great importance and potential benefit. I refer to the study of the causes of diabetic fatalities in the community, in which a start has been made in several places, including Philadelphia and Cincinnati. As concerns the value of medical statistical studies of this nature, one should note the remarkable reductions in maternal mortality in many cities achieved as the result of a program of study of the causes of maternal deaths and the institution of a program to correct the faults disclosed. Progress against appendicitis also has been helped by statistical studies of community experience. In like manner, comparable programs in the field of diabetes conducted in cities or urban areas throughout the country should be effective in reducing the number of deaths from diabetic coma and even of those from diabetic gangrene. The statistics are, of course, not the cure for the situation, but they afford a solid basis of fact on which programs of public and professional educational efforts can be established.

A fundamental condition of reliable statistics on diabetes in clinical practice is a set of good records. There are required an adequate general record form on the history of the patient and subsidiary forms that give sufficiently detailed facts regarding his status from time to time and the methods of treatment used in diabetic emergencies. I urge you to look over the forms used at this and other leading clinics to see that your own records contain at least the essential items of information and that these records are complete and systematic. A greater degree of standardization in record forms than has yet been achieved is desirable. Further efforts along these lines should be encouraged.

One of the greatest needs in the field of diabetes, as well as in many fields of medicine, is long-range study of results of treatment. This means adequate follow-up of large numbers of patients. A fundamental consideration in such studies is that the follow-up be as complete and thorough as it is possible to make it. A 100 per cent result is desirable but, of course, not always practicable. Nevertheless, it should be the goal. In the follow-up studies of cases at the George F. Baker Clinic, all but 1 or 2 per cent of the patients have been located. The achievement of good follow-up results is largely a

rate It is interesting to observe, however, that at most ages up to fifty-five, Negroes have appreciably higher death rates from diabetes than do Whites of the same age After fifty-five, the situation is reversed Among older people, the rates for Whites are double those for Negroes, or even more

There is a distinct difference between the sexes with regard to the relative mortality from diabetes according to color The rate for white females is only 3 per cent higher than that for Negroesses, whereas the rate for white males exceeds that for Negroes by nearly 40 per cent But as between city and country, females exhibit a notable difference according to color, the rates for Negroesses in all classes of cities being higher than those for white females, whereas in the rural areas the rates for white females are appreciably higher than those for Negroesses

There are marked regional differences in the mortality recorded from diabetes The rates are generally highest in the industrialized northeastern section of the country and lowest in the South and Southwest Differences in the rates in part reflect differences in the age makeup of the population, and when these are allowed for the gap between the highest and the lowest states is appreciably narrowed

A recent analysis of the crude or unadjusted rates shows that the increase in diabetes mortality is a country-wide phenomenon⁹ Comparison of the figures for 1940-1942 with those for 1930-1932 shows, curiously enough, that the increase has generally been most rapid in the states with the highest rates

INTERNATIONAL COMPARISONS

There is comparatively little information on the trend of diabetes abroad since the war began Consequently, any comparisons of this nature must chiefly rest on the situation before the war At that time, the United States had the highest mortality from diabetes among the nations of the world Generally speaking, the next highest death rates were recorded in certain countries of western Europe The rate in Canada is appreciably less than that in this country, but a great part of the difference between the two countries is attributable to the younger average age of the Canadian population In Europe the highest rates in prewar years were recorded in Denmark, Germany Switzerland, Holland, England and Belgium The rate in France was considerably lower, but French vital statistics are notoriously inaccurate with respect to causes of death The recorded death rates in southern and eastern Europe were extremely low This applies likewise to the few countries in Central and South America and to the few areas of the Orient for which figures are available In contrast, the white populations in the English colonies and dominions show rates that are comparable to the figures in western Europe

Prior to the war, an increase in diabetes death rates was practically a world-wide phenomenon in all the countries for which long-term records were available It is notable, however, that after the use of insulin began, there was a sharp reduction in the rates among children and young adults in practically all the countries for which statistics are available As in this country, the upward trend of the death rate at all ages combined reflected the increase in rates at the later ages of life

TREND OF DIABETES IN WARTIME

It was noted during World War I that there occurred an appreciable fall in the diabetes death rate in countries whose civilian populations were severely affected There is comparatively little information on this matter for World War II In the United States, Canada, Australia and New Zealand, the war had relatively little effect on the diabetes death rate In England, on the other hand, the death rate from diabetes fell more than 20 per cent.

SIGNIFICANCE OF GEOGRAPHICAL VARIATIONS IN DIABETES

Many factors are responsible for the great range of variation in diabetes mortality, and presumably in morbidity also, from state to state in this country and from one country to another throughout the world Particular mention has been made of such factors as the sex and age composition of populations In general, it will be found that the reported mortality and prevalence of diabetes are greatest where the highest standards of living are found and where the general level of medical care and medical practice is farthest advanced

The wide differences in the reported figures, after allowance has been made for obvious factors, are still further narrowed when a special effort is made to look for the disease The survey of diabetes made in Arizona a few years ago by the state's physicians under the guidance and inspiration of Dr Elliott P Joslin showed this admirably¹⁰ Thus, whereas only two or three deaths are reported annually from diabetes among the Indians of Arizona, the survey, which covered at most only two thirds of the Indian population of the state, disclosed 73 living Indians with the disease The estimated incidence of diabetes, based on the survey, was found to be of practically the same order as that recorded in the household canvass of 1929-1931 in Massachusetts and in the National Health Survey of 1935-1936 Moreover, the distribution of diabetes in Arizona was typical of that elsewhere there were more diabetic women than diabetic men, and more old than young diabetic persons, the rate in the small population of Jews in the state was relatively high, and morbidity rates in special groups studied were comparable to those of similar groups elsewhere It is likely, therefore, that where diabetes is least fre-

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THE increasing use of Pentothal Sodium as an important anesthetic agent during major surgical procedures is well attested in the current literature on methods of anesthesia. That its optimal usefulness with the greatest measure of safety is achieved when it is employed in conjunction with supplemental anesthetic agents is borne out by reports relating to such conjoint use or by those that discuss in passing the supplemental use of other agents. My¹ previous report discussed the combined use of intravenous Pentothal Sodium and local nerve block (splanchnic) in upper abdominal surgery. In this earlier study, in which a new splanchnic needle guide was described, the two major purposes sought by the novocain nerve block were, first, to provide flaccid paralysis of the rectus abdominis muscle and second, to obliterate the visceral sensory impulses by splanchnic nerve block. By this rational supplementation of Pentothal Sodium with novocain block, a sharp reduction in the quantity of the former required for anesthesia was accomplished.

As surgical experience under Pentothal Sodium is extended, it becomes more and more apparent that one is dealing with an unusual opportunity to study accurately the precise physiologic background of surgical anesthesia in human beings. This premise turns on the evident dominance of the neurogenic reflexes initiated by surgical trauma during Pentothal Sodium anesthesia in reflexly activating the respiratory center, on the specificity of the respiratory response to the surgical reflexes arising from the segmental subdivisions of the terminal cerebrospinal nerves — cervical, thoracic, lumbar and sacral, and finally on the repressive action of Pentothal Sodium on the reflexly activated center.

The first site of pharmacologic action by Pentothal Sodium is the cerebral cortex, whereby unconsciousness supervenes, the second site appears to be the thalamus, whereby all reflex motor response to surgical trauma is controlled as a result of suppression in this relay center of all sensory impulses directed toward the cortex, the third site of action is the respiratory center, whereby, in the absence of reflex stimulation from surgical trauma, there is a completely smooth graded depression of respiratory activity. Under the conditions of a surgical operation, however, painful (noxious) stimuli of constantly varying intensity are conducted from the

field of operation over the afferent limb of intact reflex arcs to the respiratory center. Depending on whether the inspiratory or expiratory neurons are specifically activated, the afferent limbs of the arcs carry back impulses that alter the character of respiration in a specific manner. Thus, the effective administration of Pentothal Sodium as an anesthetic agent resolves itself into an effort to achieve an optimal yet safe balance between the depressing action of this drug on the reflexly activated respiratory center and the stimulating action of neurogenic stimuli impinging on it that have been initiated by trauma in the field of operation. The goal sought in effectuating this balance is that of respiratory quietude without undue depression of respiration.

The introduction of novocain nerve block in anesthesia under Pentothal Sodium is directed at strategically placing the solution so as to interrupt transfer of noxious afferent stimuli centrally, thus minimizing the reflex stimulation of the respiratory center. By such a physiologic maneuver the intermittent demands for increased administration of Pentothal Sodium are eliminated and the total overall demand for the drug is sharply reduced. My experience during the last two years with the systematic combined use of these two methods of anesthesia has sustained experimentally in human beings the following generalization made in 1945 by Gordh:² "The more the physiology of anesthesia is studied, the more strikingly becomes the predominance of the part played by respiration. Indeed the physiology of respiration may be said to dominate the physiology of anesthesia."

The present study continues the report of my experiences with the combined use of Pentothal Sodium and local nerve block as a method of anesthesia in major surgical procedures. The present report specifically discusses the use of intravenous Pentothal Sodium combined with intercostal nerve block in the performance of radical mastectomy for carcinoma of the breast. It is based on a comparative study of two groups of cases. The first group consists of four radical mastectomies performed under Pentothal Sodium alone. The second group consists of six radical mastectomies performed under Pentothal Sodium and supplemental intercostal novocain block. An interesting result of the combined method is that the surgeon becomes an active participant in the production of the anesthesia, since all novocain blocking is carried out by the surgeon via a transincisional approach after the incision has been made. By this method the surgeon may

*Read by title at the postponed annual meeting of the New England Surgical Society, Boston, February 6, 1946.

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matter of resourcefulness and ingenuity in locating difficult cases. Success in follow-up studies can be facilitated by preparing for them well in advance. It helps, for example, if the patient knows that such studies are contemplated or being made and that an effort will be made to check his progress periodically. It helps if, at the original visit or hospital stay, sufficient information is obtained—such details as the patient's business address in the case of employed persons, the school attended in the case of children and the given names of married women, together with the full name, age or date of birth and business and business address of the husband. In the case of patients who are referred by other physicians or who are seen in consultation, a cordial relation with these other physicians is invaluable, particularly if these men also know of one's interest in long-range studies of cases. Periodic communications with the patients or referring physicians are helpful. Finally, use may be made of outside agencies.

The importance of a high degree of completeness in follow-up studies cannot be overstressed. Failure to achieve this is a legitimate cause for questioning the validity of the results, because it is not safe to assume that untraced cases show the same general characteristics as do those that are traced, more particularly, if the number of untraced cases is disproportionate to the number of known deaths, the mortality figures are open to doubt.

Some groups are too large to make it practicable to follow up the entire number. In these circumstances, suitable sampling procedures are permissible. As an example, the last mortality tables computed for patients of the George F. Baker Clinic were based on a 25 per cent sample. Furthermore, the results of a systematically selected sample may differ widely from those based on an aggregate of unsystematic observations. An example of this is furnished by figures covering the average duration of disease and average age at death, as given in Tables 42 (page 275) and 44 (page 277) by Joslin et al.¹¹

Certain necessary precautions must be given concerning the analysis of clinical statistics on diabetes. Characteristics and results may be expected to differ among diabetic patients according to age, sex, incidence of complications and environmental factors, such as education and social status. Allowance should be made for these various factors, if possible. In any case, the general nature of the group should be described. One must also be careful to define fundamental terms or the nature of specific classes studied in order to assess results with sufficient accuracy and fairness. The definition of diabetes is not fixed. Frank cases cause little difficulty, but borderline cases, if they form a significant proportion of the series, may be the cause of otherwise unexplained differences. Similar considerations apply with regard to the definition of diabetic coma and gangrene.

In long-range clinical studies of diabetes, profitable use can be made of the life-table method of

analysis of mortality. The average duration of life from onset of diabetes to death is not an entirely satisfactory measure of the longevity of diabetic patients. This is seen most clearly with respect to diabetic children. Fatal cases among them are not typical of the group. Most diabetic children may be expected to outlive their physicians. It is therefore necessary in mortality studies of diabetic patients to consider the total population of such patients and the deaths that occur within it. From such data are computed death rates on an annual basis, in suitable categories by age and other characteristics. This method of analysis is described in a number of excellent texts and articles. Those deserving special mention are a book by Hill¹⁴ and a paper by Frost.¹⁵

* * *

It is too much to expect the physician to be a statistician with up-to-date knowledge of technical developments in this field. It is to the doctor's advantage, however, to have a knowledge of the fundamentals of statistics and statistical reasoning, and without too much trouble he can make himself familiar with a few basic statistical procedures. There are some textbooks on statistics that are especially designed for the physician, notably the volume by Hill already referred to. Those who are connected with or live near a large university would be well advised to make use of such professional statistical assistance as can be obtained there. In this way one is less likely to commit errors through faulty classification of data and to make unwarranted conclusions based on sparse data. The war has greatly stimulated work in practical and theoretical statistics. Consequently, statistical talent is now more abundant than ever before.

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As surgical experience under Pentothal Sodium is extended, it becomes more and more apparent that one is dealing with an unusual opportunity to study accurately the precise physiologic background of surgical anesthesia in human beings. This premise turns on the evident dominance of the neurogenic reflexes initiated by surgical trauma during Pentothal Sodium anesthesia in reflexly activating the respiratory center, on the specificity of the respiratory response to the surgical reflexes arising from the segmental subdivisions of the terminal cerebrospinal nerves—cervical, thoracic, lumbar and sacral, and finally on the repressive action of Pentothal Sodium on the reflexly activated center.

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field of operation over the afferent limb of intact reflex arcs to the respiratory center. Depending on whether the inspiratory or expiratory neurons are specifically activated, the afferent limbs of the arcs carry back impulses that alter the character of respiration in a specific manner. Thus, the effective administration of Pentothal Sodium as an anesthetic agent resolves itself into an effort to achieve an optimal yet safe balance between the depressing action of this drug on the reflexly activated respiratory center and the stimulating action of neurogenic stimuli impinging on it that have been initiated by trauma in the field of operation. The goal sought in effectuating this balance is that of respiratory quietude without undue depression of respiration.

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The present study continues the report of my experiences with the combined use of Pentothal Sodium and local nerve block as a method of anesthesia in major surgical procedures. The present report specifically discusses the use of intravenous Pentothal Sodium combined with intercostal nerve block in the performance of radical mastectomy for carcinoma of the breast. It is based on a comparative study of two groups of cases. The first group consists of four radical mastectomies performed under Pentothal Sodium alone. The second group consists of six radical mastectomies performed under Pentothal Sodium and supplemental intercostal novocain block. An interesting result of the combined method is that the surgeon becomes an active participant in the production of the anesthesia, since all novocain blocking is carried out by the surgeon via a transincisional approach after the incision has been made. By this method the surgeon may

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place the novocain solution strategically, precisely and visually. Many surgeons, having been trained in the technic of novocain field block, have discarded it as a time-consuming, delaying method under conditions in which the surgeon must administer it himself in the course of a heavy surgical schedule. The use of this technic by the transincisional approach and in conjunction with Pentothal Sodium, however, restores novocain field block to the status of a precise, quickly executed technic, which proves of great value in the restricted physiologic roles herein demanded of it.

The method of combined intravenous Pentothal Sodium and intercostal nerve block in radical mastectomy is essentially simple. The patient is carried into a light third stage of surgical anesthesia with Pentothal Sodium, which permits a skin incision to be made. In this study the drug was administered in a 1 per cent solution according to the fractional drip method previously discussed. Using the Greenough modification of the Rodman incision, the posterior axillary incision is made and carried down to the ribs and intercostal muscles for the entire length of the operative field. The skin and subcutaneous tissues are dissected posteriorly beyond the point of emergence of the lateral cutaneous branches of the intercostal nerves. With the fingers of the left hand identifying each rib successively from the eighth or ninth upward to the fourth, a needle is advanced under the lower border of each rib until it penetrates the compartment between the external and internal intercostal muscles in which each intercostal nerve runs, and here 2 or 3 cc of a 1 per cent solution of novocain is deposited. The axilla is then dissected sufficiently to expose the upper four ribs and to identify and protect the axillary vessels and nerves, following which the four upper intercostal nerves are similarly novocainized. The deposition of novocain should be made posteriorly to the midaxillary line, which is the point of emergence of the lateral cutaneous branches of the intercostal nerves. By this transincisional method, a quick, accurate blocking of the intercostal nerves under vision may be easily accomplished in two or three minutes. The mastectomy may then be completed with need of but little more Pentothal Sodium.

In the first group of 4 patients, to whom Pentothal Sodium alone was administered without the use of nerve block, the drug had to be administered at the average over-all rate of 23 mg a minute for the duration of the entire procedure (induction, operation and closure). In the second group of 6 cases, in which Pentothal Sodium was supplemented by transincisional intercostal nerve block performed by me, the administration of the drug was sharply reduced to an average over-all rate of only 13 mg a minute, a reduction of nearly 50 per cent. In 1 case following establishment of the intercostal block, no further administration of Pentothal Sodium was required. In all cases in which intercostal nerve

block was established, minimal additional amounts of the drug were needed following the initial induction dose. As an example, a patient required 1 gm. (100 cc of 1 per cent solution) of Pentothal Sodium for induction, whereas after establishment of the intercostal block only 200 mg (20 cc) was needed over a period of one hour for the entire mastectomy. Although the number of cases in each group is small, nevertheless the dramatic reduction in this rate of utilization of Pentothal Sodium validates the conclusions drawn as to the importance of the supplemental use of local nerve block in the operative field. The significance of the intercostal block from the viewpoint of the physiology of surgical anesthesia is that the noxious impulses from the operative field were blocked, they were not conducted centrally and neither impinged on nor stimulated the respiratory center. As a consequence, patients were carried in a light plane of anesthesia with quiet, unstimulated respiration during the entire procedure.

DISCUSSION

The conclusion derived from these successive studies is that the fundamental base from which a consideration of the physiology of surgical anesthesia may properly proceed is the dominance of specific surgical reflexes in so far as they stimulate the respiratory center and activate the respiratory mechanism. This concept accurately integrates with the increasing recognition in recent years of the importance of neurogenic stimulation of the respiratory center, as contrasted with its chemical stimulation. The painful (noxious) stimuli of surgical trauma, whether from the somatic or visceral zones, are conducted centrally and impinge on the respiratory center, stimulating it to activity, preponderantly on the inspiratory or on the expiratory side. The type of response depends on the peripheral segmental representation of the cerebrospinal nerves in the field of trauma — whether cervical, thoracic, lumbar or sacral. The anatomic specificity of reflexes from the different segmental areas of operation has been recorded and demonstrated by me with pneumographic recordings.

The segmental character of the respiratory response to neurogenic stimuli initiated by surgical trauma may be briefly outlined as follows:

Cervical segment Little stimulation of the respiratory center is evident from surgical trauma in this area, as evidenced by observations made during thyroidectomies. Few opportunities were available for studying respiratory response during operations on the upper extremities. In 1 case, traction on an exposed median nerve sharply stimulated the center.

Thoracic segment The wide area of the body supplied segmentally by the intercostal nerves extends from the neck to the symphysis pubis. In all operative procedures in this segmental zone, in the somatic plane, the same characteris-

tic respiratory response is elicited and may be strikingly recorded by a pneumograph. There is a transient stimulation of the inspiratory phase of respiration. There is a sharp and prolonged stimulation of the expiratory phase, characterized by a succession of respiratory cycles in which the phase is intensified and prolonged for four to twelve seconds. In a few cases traction on the upper abdominal viscera has produced a nearly complete expiratory arrest. This prolongation of expiration is due to the fact that the expiratory phase has been converted from a passive to an active phenomenon. The accessory muscles of respiration, particularly the rectus abdominis, internal and external oblique and transversalis muscles, are reflexly and fully activated during expiration, so that they retract the lower ribs downward and inward during the expiratory phase for varying periods of time. In light planes of anesthesia this effort may be accompanied by an expiratory grunt. Increased quantities of Pentothal Sodium depress the more sensitive and reflexly stimulated expiratory neurons, doing so far in excess of the drug's depressing action on the inspiratory neurons. By this action the distorted inspiratory-expiratory ratio, which may be 1.5 or 1.6, is normalized and restored to the usual 1:1 ratio. At this point the accessory muscles are no longer activated, the expiratory phase returns to a passive state, and respiratory quietude again prevails. The reflexes from the thoracic segment when initiated in the skin and subcutaneous tissues may be blocked by novocain infiltration or by inhalation of nitrous oxide and oxygen. In the field of radical mastectomy they may be interrupted by an intercostal nerve block, when arising from the subdiaphragmatic visceral zone they may be interrupted by splanchnic block, and when arising from manipulation of the bowel they may be interrupted by mesenteric block. The peritoneal traction reflex, initiated during closure of the incision and transmitted centrally by the somatic intercostal nerves, may be easily suppressed by small quantities of cyclopropane or of nitrous oxide and ether. The more profound visceral and peritoneal traction reflexes are not controlled by inhalation of nitrous oxide and oxygen alone with Pentothal Sodium.

Lumbar segment The reflex stimulation of respiration from the zone of lumbar-nerve distribution is mild as compared with that from the thoracic zone. There is a mild increase in the rate and amplitude of both inspiration and expiration, the normal ratio of the two phases is preserved, expiration does not become an active phase, so that the accessory abdominal muscles of respiration are not activated, and abdominal quietude is consequently not disturbed. The lumbar reflex may be demonstrated by traction on the superior hypogastric plexus during a pre-

sacral neurectomy. This reflex may be obliterated by novocain block above the level of traction. In clinical surgery this reflex is not often encountered. It is generally seen in the presence of extensive pelvic inflammatory disease or endometriosis, when the adnexa have to be forcibly separated from the pelvic parietal peritoneum. In the somatic area the reflex may be noted during operations on the lower extremities in the zones of lumbar-nerve distribution. This reflex is quite easily controlled by small additional quantities of Pentothal Sodium.

Sacral segment The sacral reflex is strikingly characteristic and different from the reflexes elicited in the other segmental zones. It arises only from the deep pelvic zones in cervicovaginal regions in the female and in the prostatic regions in the male. During pelvic surgery strong traction on the cervical region may evoke a single prolonged inspiratory effort, accompanied by a loud inspiratory moan due to reflex laryngospasm. No succession of repeated respiratory responses is established as is characteristic of the thoracic and lumbar reflexes. The sacral reflex may be blocked by novocain placed deeply in the curve of the sacrum or by infiltration of the uterosacral ligaments at their point of attachment to the cervix. These ligaments have in this manner been experimentally revealed as the pathway for transfer of the sensory nerves responsible for this distinctive sacral reflex. This reflex may also be elicited from trauma to the penis during a circumcision, by impulses transmitted over the dorsal nerve of the penis to the internal pudendal nerve and thence to the sacral plexus. In the somatic areas the reflex may be elicited over the saddle area of distribution of the sacral nerves in the region of the anus, inner thigh, vulva and scrotum. The sacral reflex has no significance in so far as quietude of the operative field is concerned. Its constant repetition may, by virtue of its noisy laryngospasm, be a source of annoyance to the surgeon and the anesthetist.

SUMMARY

Further experiences with the use of combined intravenous Pentothal Sodium and local nerve block anesthesia are presented. A previous report described the sharp reduction in the rate of utilization of Pentothal Sodium for upper abdominal surgery following the supplemental use of splanchnic nerve block. In the present study a comparable sharp reduction in the rate of utilization of the drug during radical mastectomy for cancer of the breast following the supplemental use of intercostal nerve block is reported. This observation is related to the physiology of surgical anesthesia in so far as the quantity of Pentothal Sodium required for a satisfactory anesthesia is directly proportionate to the amount needed to repress the activated respiratory

center, which has been reflexly stimulated to over-activity by noxious stimuli arising from the operative field. By the strategic use of novocain block by a simplified transincisional approach, these stimulating impulses are prevented from reaching and activating the respiratory center. Thus, the excessive demand for Pentothal Sodium to control the reflexly stimulated center sufficiently to restore respiratory quietude is circumvented.

A brief résumé of the specific segmental character of the surgical reflexes and respiratory response evoked from the different body areas has been given, in so far as they evoke a characteristic response from the respiratory center. These have been recorded by pneumographic tracings.

A general statement with reference to the combined use of the two methods of anesthesia may be made. On the basis of a physiologic integration of methods, the Pentothal Sodium induces quiet sleep that is free from any excitement, it provides a quiet respiration, by repressing the stimulation of the respiratory center from the less intense surgical reflexes, it provides a comfortable recovery period singularly free from nausea and vomiting and from

pulmonary complications. Strategic transincisional novocain block provides relaxation of muscles, it may be used to block massive reflex impulses from stimulating the respiratory center, — intercostal, splanchnic, mesenteric or pelvic block, — thus reducing the demands for large quantities of Pentothal Sodium. The terminal use of small quantities of cyclopropane or of nitrous oxide and ether to control the peritoneal traction reflex at the time of closure of the incision eliminates the final large peak demand for Pentothal Sodium, thus contributing to the early awakening of the patient.

This rational integration of methods in terms of the basic physiology of surgical reflexes and respiration during anesthesia and surgery has provided an eminently safe and satisfactory method of anesthesia for over 70 per cent of general surgical operations.

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MEDICAL PROGRESS

ACTIVE IMMUNIZATION (Continued)

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PERTUSSIS

Despite the fact that infant deaths from pertussis have decreased 70 per cent in the last forty years, it remains the most frequent cause of death among the acute contagious diseases of early childhood. "The concentration of deaths in the first two years of life, especially under six months, is constant for all parts of the United States."¹⁹³ A recent editorial¹⁹⁴ points out that in Massachusetts from 1924 to 1943, 58 per cent of all deaths from this disease occurred in the first year of life, and 84 per cent in the first two years. Furthermore, the disease in older children, although rarely fatal, is frequently prolonged and debilitating, and involves much time lost in isolation and away from school. Hence there is ample justification for the numerous attempts that have been made to control the disease by means of immunization.

During the last fifteen years, beginning with the work of Leslie and Gardner¹⁹⁵ on the antigenic phases of *Haemophilus pertussis*, the principles underlying artificial immunization against whooping

cough have been sufficiently elucidated to make possible the production and use of vaccines that, in most of the studies reported, protected a large majority of the persons immunized. The development of pertussis vaccination up through 1942 has been reviewed by both Lapin¹⁹⁶ and Felton and Willard.¹⁹⁷ With few exceptions, the studies reviewed have demonstrated in large groups of children that the communicability rate of pertussis in persons vaccinated with 70 to 120 billion killed, whole, virulent pertussis bacilli is much less than the expected rate as determined by experience in unvaccinated children. Similar results are found in the more recent reports of Bustamante,¹⁹⁸ Galvin and Wampler¹⁹⁹ and Garvin.²⁰⁰ Moreover, attempts to evaluate the severity of the pertussis occurring in both groups, generally revealed that fewer severe cases occurred in the vaccinated than in the control groups. These findings have in general indicated that vaccination resulted in from 75 to 90 per cent protection. Such field studies have been criticized, on the basis that the unvaccinated groups used for comparison were not valid controls.²⁰¹ This criticism has in some cases been justified, and it is fair

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to demand that the study and control groups be submitted to an independent test of random selection, such as a comparison of the incidence of other communicable diseases in both groups.^{202, 203} An interesting method of analysis is that of Sargent and Merrell, which has been applied to pertussis immunization by Weiss and Kendrick.²⁰⁴ They compared the incidence of pertussis among immunized and nonimmunized children under ten years of age reported during a given period as having contracted scarlet fever, measles, chicken pox or pertussis. From these data and from the pertussis immunization files, it was possible to compare the expected incidence of pertussis, if the immunization had been of no value, with the actual incidence. Only 15.8 per cent of the expected cases occurred in the immunized group. In passing it should be noted that the 34.8 per cent attack rate, sometimes cited²⁰⁵ from Kendrick and Eldering's major study²⁰³ as being in essence a failure, occurred among children experiencing intimate exposure to the disease — the control group showing a communicability rate of 89.4 per cent. To be fairly evaluated, such figures should be compared with similar studies of the effectiveness of a generally accepted bacterial vaccine in the presence of an equally high attack rate among the controls. Such a comparison would be difficult, for few bacterial infections occur under conditions leading to a 90 per cent attack rate.

Except for the widely discussed study of Doull et al.²⁰⁶ in Cleveland ten years ago and the subsequent unfavorable one of Siegel and Goldberger,²⁰⁷ most reports indicate that a significant degree of protection is obtained with pertussis vaccine. The failure of the Cleveland immunization program has been generally attributed to the fact that the vaccine was washed in distilled water, a procedure since suspected of being injurious to the antigen and not employed in any other major study until the recent British trial of pertussis vaccine reported by McFarlan et al.²⁰⁸ who apparently used an ample vaccine dosage as judged by bacterial counts and whose study was well controlled. Among 350 vaccines the incidence of pertussis scarcely differed from that in the control group. On the basis of these findings and those of Doull et al. and Siegel and Goldberger, a concurrent editorial²⁰¹ concluded that the favorable reports of the last ten years are open to question. The editorial ignored or minimized the facts that the British vaccine was grown on horse-blood medium, which has been shown to favor rapid loss of antigenicity in *H. pertussis*,²⁰⁹ that the studies of McFarlan and Doull and their associates — the only two in which the vaccine was washed in distilled water — represent two of the three important failures of pertussis vaccination in the last decade, and that the British vaccine was held in phenolized distilled water at icebox temperature for a week, which would presumably have accentuated whatever injury may be done by distilled water. The bur-

den of proof appears to lie with those who do not consider washing in distilled water to be harmful, in any event, a comparable study is now being carried out in England, using a generally accepted vaccine of American make.

Undoubtedly there is considerable room for improvement in pertussis vaccines and vaccination. The protection rate, although it may be highly satisfactory from an epidemiologic point of view, is not entirely so to the practicing pediatrician. The chances of protection cannot well be enhanced by an increase in the dosage of the standard vaccine, which is already high in volume (up to 7 cc in some schedules), in numbers of bacteria (70 to 120 billion) and in numbers of doses (three to five), also, the procedure is followed by a relatively high incidence of local and general reactions. On the other hand, the dosage cannot wisely be reduced. There are, however, various ways of increasing the effectiveness per unit dose of the vaccine. Lapin et al.,²¹⁰ Miller and Saito,^{211, 212} Coppolino²¹³ and Mishulow et al.²¹⁴ favor intervals of two to four weeks between doses. Although no comparative clinical studies have proved that a longer interval yields superior protection, such a supposition is reasonable in the light of numerous studies on other immunizing procedures cited elsewhere in this review.

Alum-precipitated pertussis vaccine was introduced several years ago by Harrison, Franklin and Bell,²¹⁵ who found a single dose of 10 billion organisms prepared in this fashion to be insufficient, Bell²⁰² subsequently showed, however, that two such doses at an interval of four weeks gave a high level of protection, and similar results were obtained by Kendrick.²¹⁶ The use of aluminum hydroxide absorption has recently been reported,²¹⁷ and may represent a possible improvement over alum precipitation, since the reactions appear to be somewhat milder.

Until recently, all successful pertussis vaccines were prepared on some modification of the classic Bordet-Gengou type of blood-starch-agar medium, either human (Sauer) or sheep (Kendrick) blood being used. Hornibrook²¹⁸ had shown that *H. pertussis* could be sustained in Phase I for several generations in a liquid medium of relatively simple composition. Wilson,²¹⁹ Taylor and Farrell²²⁰ and Cohen and Wheeler²²¹ introduced successive improvements, so that rapid adequate growth of a virulent, antigenic form of the organism can be obtained in this type of medium without the necessity of introducing red blood cells or foreign protein in any other form. Such a medium approaches the ideal for its purpose, since it minimizes the chances of inducing untoward reactions to substances of high molecular weight while retaining a maximum of the antigenic material present in the original growth.

The numerous attempts to evaluate the significance of the toxins of *H. pertussis* have been well reviewed by Lapin.¹⁹⁶ Several recent studies lend sup-

port to the long established belief that a toxic factor contributes to the pathogenesis of pertussis Sprunt and Martin²² showed that the edema, necrosis and mononuclear reaction that can be induced in rabbit lungs by pertussis toxin could be prevented by an antitoxin produced in rabbits Ospeck and Roberts²³ found that the same antitoxin furnished more effective protection against live *H. pertussis* cultures than an antibacterial serum Evans,²⁴ in a carefully controlled study, presented evidence that parenterally administered pertussis antitoxin offered little protection against pertussis bacilli introduced intranasally, whereas intranasally applied antitoxin exerted a more marked protective action than an antibacterial serum Such findings suggest that antitoxic titers in human beings should bear some relation to resistance to pertussis, but a study in patients convalescing from pertussis showed that detectable titers were rarely found²⁵ Moreover, an intradermal susceptibility test based on Streaus's²⁶ endotoxin failed to reveal a definite correlation either with a history of pertussis or with previous vaccination²⁷ Finally, the detoxified pertussis antigen developed by Roberts and his associates, when submitted to a recently reported field trial, did not appear to afford significant protection²⁸ One must conclude, therefore, that the role of the toxic factor in susceptibility or resistance to pertussis infection has yet to be elucidated

The combination of pertussis vaccine with other antigens was first suggested ten years ago by Bordet²⁹ It has been shown in animals³⁰ and in man³¹ that the two antigens exert no mutual interference as judged by laboratory measurements of antibody response Kendrick³² and Sauer³³ and their associates carried out field studies in which alum-precipitated combined pertussis vaccine and diphtheria toxoid was used Both groups found that the mixture gave protection against pertussis and yielded a high proportion of Schick-negative subjects Lapin³⁵ and Miller and Saito³² suggested the addition of tetanus toxoid to the immunization against diphtheria and pertussis, considering various combinations and schedules that could be used with this in view³² Lapin concluded that the best results, as judged by laboratory tests, and the fewest reactions were obtained by the administration of the pertussis vaccine alone and the combined toxoids as separate injections either concurrently or later, he³⁶ noted elsewhere that the triple combination induced a large percentage of severe reactions and alum abscesses Many physicians have confirmed his observation that the combined irritating effects of pertussis vaccine and alum — perhaps potentiated by the presence of toxoid — tend to produce an undesirably high incidence of local inflammatory reactions and not a few abscesses Hamilton and Knouf³⁷ recently reported the use of a fluid triple preparation, with apparently excellent results and few reactions Such a prepara-

tion may offer a satisfactory means of inducing simultaneous immunity to diphtheria, pertussis and tetanus, with a minimum of injections and reactions Some clinicians, however, preferring to follow Lapin's findings, administer the pertussis vaccine first and the combined toxoids subsequently This schedule has the advantage of placing the pertussis immunization at the earliest possible date, when it is most needed Use of triple vaccine-toxoid at this early date has the disadvantage that the infant's response to diphtheria toxoid is likely to be less satisfactory than it is a few months later³⁸

The use of a booster dose to maintain or restore immunity to pertussis in a previously vaccinated subject has an excellent theoretical basis but has not yet been submitted to any adequate clinical trials Nevertheless, the antibody responses following booster injections are so striking and so well sustained³⁸ ³⁹ that there is every reason to believe that the procedure is a valuable one The analogy with other immunization procedures that have been more thoroughly studied suggests that the response to a booster dose of pertussis vaccine most frequently reaches its peak in ten to fourteen days and is therefore effective in protection just before or perhaps even after actual exposure On the other hand, primary vaccination against pertussis is of doubtful value during an epidemic or after exposure Several studies suggest that some degree of protection is obtained even under these circumstances,¹⁹ ⁴⁰ ⁴¹ but such findings are by no means unanimous⁴²

The protection of young infants against pertussis has presented a particular problem, ever since it was shown that the response to vaccination — as with most other immunizations — was less satisfactory in the first than in the second half of the first year of life Sauer's⁴³ experience supported this finding and led him to recommend against immunization in the first six months of life Sako et al,⁴⁴ however, reporting on the immunization of almost 4000 infants less than three months old, observed a communicability rate, in family exposures, of only 19 per cent, in contrast with one of 92 per cent in the control group Sako's exceptionally good results, which may not be reproducible in a more inclement climate, appear to justify immunization against pertussis at an earlier age than has been customary

Another attack on this problem is the immunization of pregnant mothers, recommended by Cohen and Scadron,⁴⁵ Mishulow et al⁴⁶ and Kendrick and her co-workers⁴⁶ The antibody titers obtained in mothers and transmitted to their infants suggest that some protection is induced by this method

TYPHOID FEVER

Evidence of the efficacy of typhoid vaccination is found in several recent reports Martel⁴⁷ describes a localized typhoid epidemic in an outlying district of the Province of Quebec, where the number of

ases fell from 35 in the year before vaccination was begun to 17, 5 and 1 respectively in the succeeding three years. Callender and Luippold,²⁴⁸ Murphy et al.²⁴⁹ and Duncan and his associates²⁵⁰ report outbreaks of typhoid fever among significantly large vaccinated and unvaccinated groups, subject to identical and simultaneous risks of infection, so that the efficiency of the vaccine could be determined. The respective incidence of the disease in each outbreak was as follows: 55 cases among 4000 vaccinated soldiers as against 56 cases among 800 unvaccinated civilians (14 vs 7.0 per cent), 8 cases among 170 vaccinated civilians as against 61 cases among 531 unvaccinated civilians (4.7 vs 11.5 per cent), and 1 case among 180 vaccinated SPARS as against 17 cases among 194 unvaccinated civilians (0.5 vs 8.7 per cent).

It is apparent that immunization against typhoid fever — like virtually all other immunizations — affords a marked but not absolute degree of protection. As one would anticipate, numerous reports of typhoid fever in immunized persons have appeared during recent years.²⁵¹⁻²⁵⁴ All reports stress the atypical nature of the disease in immunized persons, and two observers report a relatively high incidence of complications in such cases.^{252, 254} — a finding that may well be related to the difficulty, and hence the delay, experienced in making the diagnosis. Gav,²⁵⁵ almost thirty years ago, wrote

It may well be questioned why further modification of typhoid vaccine should seem necessary in view of the extremely good protective results that have already been obtained in certain large groups of individuals. The only answer to such questions is and must ever remain that the theoretical considerations based on the understanding of underlying principles will ever precede all practical advances.

Although Smith and Reagh²⁵⁶ had called attention to the dual nature of certain bacterial agglutinins as long ago as 1903, little attention was paid to this phenomenon until the demonstration of the separate identity of O and H agglutinins by Weil and Felix.²⁵⁷ Arkwright²⁵⁸ later demonstrated the close relation between smoothness and virulence of cultures of *Eberthella typhosa*, and their ability to produce O agglutinins and confer protection on guinea pigs through vaccination. Grinnell showed that vaccines prepared from smooth virulent cultures induced bactericidal antibodies²⁵⁹ and protected mice against lethal quantities of live bacilli²⁶⁰ to a degree far beyond what could be achieved by vaccination with rough, avirulent cultures. These findings were followed by the studies of Perry and his associates²⁶¹ of the Royal Army Medical Corps, and Siler and his co-workers,²⁶² of the United States Army Medical Corps, as a result of which virulent strains were substituted for the classic Rawlings strain used in vaccine production. The United States Army group²⁶² subsequently carried out numerous and fundamental studies on methods of evaluating typhoid vaccine.

It is of practical consequence to the physician that these studies and similar investigations elsewhere have provided the basis on which the National Institute of Health four years ago set up minimum requirements for typhoid vaccine entering interstate commerce in the United States.²⁶³ These provide that such vaccines shall be prepared from cultures derived from or antigenically equivalent to the Panama 58 strain of *E. typhosa*, which was selected from among many strains for its high degree of virulence, antigenic composition and immunizing power and which immunizes successfully against strains of *E. typhosa* collected from widely separated parts of the world.²⁴⁸ The other principal feature of the minimum requirements is a mouse-vaccination test that, although simple to perform, is sufficiently rigid to exclude the poorer grades of vaccine. Griffiths,²⁶⁴ Luippold²⁶⁵ Shaffer et al.²⁶⁶ and others have refined the protection test so that it can be used to distinguish relatively small differences in potency, such as those resulting from minor variations in methods of preparing vaccines. It should be noted that the satisfactory performance of a mouse-protection test for typhoid vaccine depends on the use of the mucin suspension technic^{267, 268} and that tests performed without the use of mucin, although of some value, are less easy to interpret, thus the low value that Felix²⁶⁹ placed on the protection test might have been modified had he employed the mucin technic.

There is no unanimity regarding the best procedure to be employed in the preparation of typhoid vaccine. The classic method is to heat the vaccine at 53 to 56°C for about sixty minutes and then to add 0.25 per cent Trikresol or an equivalent phenolic preservative. Both heat and phenol are known to be deleterious to many antigens, and a controversy has long existed concerning their effect on typhoid vaccine. Rainsford^{270, 271} Siler and his co-workers,²⁶² Felix,²⁶⁹ Ungar et al.,²⁷² Shaffer et al.,²⁶⁶ Levinson²⁷³ and others employed silver ion, formalin, acetone, chloroform, alcohol, Merthiolate and ultraviolet irradiation for inactivation of the vaccine, the product obtained being in most cases superior in immunizing potency to the classic preparation. Meanwhile, scattered attempts have been made to prepare and evaluate typhoid vaccines modified by the addition of alum²⁷⁴ or the inclusion of an endotoxoid factor^{275, 276}, sufficient data to judge the merits of these modifications are not yet at hand.

The preparation of purified typhoid antigens, free from the extraneous substances present in the whole bacillus, has been the object of numerous investigations and, if accomplished, might aid in the elimination of the untoward side reactions that are the bane of typhoid vaccination. Such an approach must be preceded by a precise definition of the various antigens required for effective immunization and of the role played by each. It was shown some years ago²⁵⁸ that, of the two classically described O and H antigens, only the former was definitely con-

cerned in protection against typhoid infection Felix and Pitt²⁷⁷ described a third antigen, closely associated with virulence and designated by them as the V₁ antigen, whose role in protection against infection has not been clearly defined, although it has been shown to possess high immunizing potency in mice.^{278, 279} Felix proposed the concept that it stimulated resistance to bacterial invasion, whereas antibodies to the O antigen protected the host against the toxic effect of large quantities of typhoid bacterial substance. This concept has been supported by quantitative studies.²⁷⁹ Nevertheless, the high efficiency of typhoid vaccines, most of which are prepared in a manner supposed to destroy the delicate V₁ antigen, remains to be explained.

Various investigators have prepared relatively pure concentrates of the immunizing antigenic substance of typhoid bacilli.²⁸⁰⁻²⁸⁶ Such preparations consist primarily of a complex polysaccharide, with an immunizing potency several thousand times that of the original vaccine, weight for weight. This active substance, which is stable and filterable, appears to be somewhat less toxic, per unit of immunizing potency, than the original vaccine. Treffers²⁸⁷ recently showed that the toxicity of this substance can be greatly reduced by acetylation with acetic anhydride. Such preparations, because of their inherent advantages, would rapidly become generally used except that, as with chick-embryo smallpox vaccine, they must compete against a product that has been amply proved to be effective against actual clinical infection. It will therefore take a bold spirit to induce the medical or public-health professions to try purified typhoid antigens on a significantly large scale.

The standard dosage of typhoid vaccine — 0.5, 1.0 and 1.0 cc subcutaneously, usually at intervals of seven to ten days — has scarcely been questioned since its establishment. Bensted²⁸⁸ advocated diminishing the dosage for civilian immunization, simply to reduce the incidence of side reactions. The ritualistic observance of the usual interval is no longer adhered to, and the United States Army regulations now permit the resumption of an interrupted course of immunization instead of repeating it in its entirety, as was formerly required. Although evidence is lacking, extensive experience with other types of immunization indicates that longer intervals between doses of typhoid vaccine would doubtless give an immunity superior to that obtained with one-week intervals.

Intradermal immunization has had its advocates since it was first proposed by Tuft.²⁸⁹ Of the numerous subsequent studies of this method,²⁹⁰⁻²⁹⁴ all but two^{291, 294} evaluated the results only by agglutinin titrations. All observers reported milder reactions following intradermal immunization, Van Gelder and Fisher,²⁹² who obtained poorer agglutinin titers following intradermal injection, nevertheless considered the reduced reactions sufficient to render the

intradermal method superior to the subcutaneous method for typhoid immunization. Tuft²⁹¹ and Luippold²⁹⁴ employed mouse-protection tests for evaluating the results. Their findings conflict, and further studies may be required to determine the usefulness of this method for primary immunization.

Largely because of the theoretical and experimental support that oral antityphoid immunization received from the work of Besredka,²⁹⁵ this method has been rather widely employed. Recent reports indicated that little, if any, agglutinin formation^{296, 297} and no detectable mouse-protective antibodies²⁹⁸ followed its use. General opinion among immunologists is that the procedure as at present employed is of little value. It is hardly surprising that a report of intranasal typhoid immunization²⁹⁹ yielded equally negative results.

Reimmunization against typhoid fever, as instituted in the United States Army a generation ago, consisted of a repetition of the initial immunizing course at three-year intervals. In the light of the knowledge of the time, this was a sound procedure. Subsequently, agglutinin studies showed that the antibody response to reimmunization was superior to that following the initial course of vaccine.²⁹⁹ This was confirmed later by mouse-protection studies,²⁹² which also demonstrated the correctness of Perry's observation²⁹⁰ that a single dose of vaccine, either 0.5 cc subcutaneously or 0.1 cc intradermally, was sufficient to reawaken a formerly established immunity. Furthermore, it appeared that such a single dose was effective even in persons who had not been revaccinated for a number of years.³⁰⁰ It is therefore generally recommended that persons who have had one course of primary antityphoid immunization no longer need to repeat a complete course periodically, but may maintain an adequate degree of protection by means of periodic single doses of vaccine, either 0.5 cc subcutaneously or 0.1 cc intradermally. The latter procedure apparently is the more effective of the two,^{292, 300} but for practical purposes the subcutaneous route is frequently adopted. To maintain a high level of immunity, such single booster doses should be administered annually,³⁰⁰ but as suggested above, almost all subjects who have had no typhoid immunization for many years show a vigorous antibody response following a single booster dose.

Combined immunization, several antigens being given in a single dose, may be said to have been established with the use of typhoid-paratyphoid A and B vaccine during World War I. Such mixtures were extended, particularly in the British armed forces, to include cholera vaccine, and favorable reports on such multiple combinations have appeared in Germany.³⁰¹ Quantitative studies on the comparative immunizing potency of such mixtures of enteric vaccines were made on typhoid-paratyphoid A and B vaccine by Longfellow and Luippold,³⁰² who observed that it appeared to produce a lower

level of antityphoid immunity than that noted in earlier studies using monovalent typhoid vaccine. Although the two studies are not strictly comparable, the findings suggest that the relative efficacy of the various combinations in current use should be re-investigated. Several years ago it was suggested, on the basis of United States Army statistics, that immunization with typhoid-paratyphoid A and B vaccine provided some protection not only against the designated infections but also against various milder forms of diarrheal disease.³⁰³ This seems to be a reasonable possibility, in the light of current knowledge of the antigenic structure of the various strains of the paratyphoid group. Longfellow and Luippold,^{304, 305} using mouse-protection tests, offered evidence that such protection is directly related to the antigens shared by the organisms. Thus it may be possible, by careful selection of organisms having an appropriate antigenic pattern and quality, to prepare a vaccine providing cross-immunity against a relatively large number of clinically infective strains. Clinical evidence of the efficacy of the paratyphoid components in preventing paratyphoid A or B fevers, however, has not been established on as sound a basis as has been done for typhoid vaccine, Syverton et al.³⁰⁶ in a recent report on an outbreak of paratyphoid A in military personnel, contributed pertinent observations on this question.

Typhoid or typhoid-paratyphoid vaccines have been combined with diphtheria or tetanus toxoids, or both,^{147, 307, 308} with no evidence of loss and some reports of definite increase in effectiveness. Such combinations have practical value for military purposes, and also, in a limited way, for certain civilian needs.

Reactions to typhoid vaccination have always represented a major obstacle to the use of this procedure, especially among civilians. As noted above, Bensted²⁸⁸ suggested that this difficulty be met by reduction in dosage, but there is no published evidence of the immunizing efficacy of less than the standard doses of the vaccine. Over twenty years ago, following the suggestion of Dr Béla Johan, of Hungary, the Massachusetts Antitoxin and Vaccine Laboratory effected a definite reduction in the incidence of reactions by centrifuging the crude vaccine, discarding the supernatant and resuspending the sediment in cresolized, buffered saline solution. Two decades later, however, the mouse-protection test showed that such a preparation possessed but a marginal immunizing potency. The method of inactivating the vaccine was revised, Merthiolate being substituted for heat and Trikresol, with a resultant marked increase in potency.²⁸⁶ No data are yet at hand to determine the comparative reactions produced by the current product. The studies of Morgan^{284, 286, 309} and others suggest that chemical separation of the toxic from the antigenic component of typhoid vaccine may be difficult if not

impossible, the final solution of the problem may therefore lie in detoxification.²⁸⁷ Some such change in the fundamental nature of the vaccine must be sought; if it is to receive the general acceptance that must at times be required.

An occasional local reaction is the appearance of a small granulomatous reaction at the site of an intradermal inoculation of the vaccine.³¹⁰ Such reactions may be of cosmetic importance in females, but are of little significance otherwise. Various other reactions are ascribed to the vaccine from time to time. The report of Toomey and Tischer,³¹¹ suggesting that typhoid vaccination may increase susceptibility to poliomyelitis, is too limited in scope to be regarded as significant without further study. The risk of inducing so-called "provocative typhoid" by vaccination in the presence of incipient infection was long maintained by some observers, being emphasized by no less an authority than Topley.³¹² Fitzgerald's³¹³ skepticism regarding this phenomenon, however, is shared by many of those experienced in the control of the disease.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

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CASE 32351

PRESENTATION OF CASE

A forty-six-year-old housewife entered the hospital because of abdominal pain.

The patient had had three pregnancies, after each of which she noticed some weakness of the legs and a staggering gait. Seven years before entry, following the last pregnancy and a subsequent panhysterectomy for placenta accreta, these symptoms persisted and gradually progressed. Numbness and paresthesia in the legs, nocturnal back pain and poor sphincter control also developed. The patient was seen at this hospital three years before entry, when neurologic examination revealed slight spasticity of the arms and moderate spasticity of the legs, without paralysis or weakness. She also had a band of hyperesthesia to pinprick from the third to the sixth rib, as well as absent vibratory sense and poor position sense in the lower extremities. The Romberg test was positive. The heel-to-skin test was poorly performed. The deep tendon reflexes were all hyperactive. The plantar reflexes were extensor on both sides, and there was a Hoffmann sign on the left. Physical examination was otherwise negative, except for some resistance to deep palpation and slight tenderness in the right upper quadrant, with a questionable freely movable mass just to the right of and extending from the umbilicus upward to the right costal margin. A diagnosis of multiple sclerosis was made, and the

patient was followed in the Out Patient Department. The symptoms continued to increase gradually, and several weeks before entry she began to notice numbness in the hands. During the year before entry a gradual increase in the size of her abdomen, accompanied by occasional vague dragging sensations, had been noticed. Ten days before entry a tight feeling had developed in the abdomen, and the dragging sensations had become painful. Four days later the patient began to have sharp pains in the right lower quadrant every time she exerted herself or moved the abdomen. These pains gradually grew worse, and the entire right side of the abdomen became tender. She also lost her appetite and ate very little, but she did not vomit. During the four days before entry the abdomen had shown a sudden further increase in size until she was unable to button her coat. She had had normal bowel movements every day, including the day of admission.

Physical examination revealed a somewhat pale woman in moderate distress. The heart and lungs were normal. A large irregular, elongated tender mass filled the entire right side of the abdomen from the costal margin to the pelvic brim. It was not possible to feel between this mass and the liver at the right costal margin. The mass appeared to move with respiration. Peristalsis was present. Vaginal examination revealed a small freely movable, slightly tender cervical stump. The neurologic findings were essentially similar to those of the previous examination, with a slight progression.

The temperature was 101°F, the pulse 88, and the respirations 18. The blood pressure was 128 systolic, 78 diastolic.

Examination of the blood revealed a hemoglobin of 12 gm and a white-cell count of 10,600, with 84 per cent neutrophils. The urine was normal.

A plain film of the abdomen revealed a considerable amount of gas and fecal material in the large bowel, particularly in one isolated loop lying in the midabdomen (Fig 1). There was an ill-defined soft-tissue mass in the right lower abdomen. In the standing position no air was seen under the diaphragm, and no fluid levels were visible within the bowel loops.

An operation was performed on the second hospital day

DIFFERENTIAL DIAGNOSIS

DR FRANKLIN G BALCH, JR May we see the x-ray films?

DR JAMES R LINGLEY In all the films there is a great deal of gas in the colon and the dilated

mass I cannot in any way connect the mass in the right side with the diagnosis of multiple sclerosis, and the nature of the right-sided mass must therefore be explained Seven years before admission a panhysterectomy had been performed According to my ideas, a panhysterectomy is a total hysterectomy, including the uterus, both ovaries and tubes. Later in the physical examination, however,



FIGURE 1 Plain Film of Abdomen

loop mentioned in the record looks like an enormously distended, dilated and inverted cecum. The mass is questionable, although there is increased density in that region. One might explain the dilatation of the cecum by the mass obstructing the ascending colon.

DR BALCH This is essentially the problem of a forty-six-year-old woman with a definite diagnosis of multiple sclerosis and a right-sided abdominal

the cervix is mentioned, and I wonder whether the ovaries were removed.

DR W P GIDDINGS We were told that the ovaries had been removed.

DR BALCH Under those circumstances an ovarian cyst can be excluded. That is the likeliest diagnosis for a tumor in the right side, except that it extended up to the costal margin.

Localized ascites is unusual, and I do not entertain that diagnosis seriously

Diseases of the liver and gall bladder must be considered. It was stated in the record that the examiner could not palpate between the liver and the mass. That does not mean that the mass necessarily arose from the liver. Echinococcal cyst in the liver is a possibility, but no mention is made about where the patient had lived and no echinococcal complement-fixation test was done, so that the data are insufficient to warrant that diagnosis.

There is a possibility that hydrops of the gall bladder was present, but the history is too long and drawn out for such a diagnosis. If the statement is correct, and I assume that it is, the patient noticed a gradual increase in the size of the abdomen for a year. The same objection holds true for empyema of the gall bladder. Furthermore, she was not sick enough for an empyema and the pain was in the right lower quadrant and not the right upper quadrant, as one would expect with gall-bladder disease, which I believe can be ruled out.

What other form of cyst or tumor could this have been? A solitary cyst of the lower pole of the kidney is a possibility. The x-ray studies do not suggest it, although sufficient gas was present to obscure such a lesion. No investigation was made of this possibility, and I expect that such a lesion would have been felt on physical examination. Cyst of the pancreas occurs higher up and is closer to the midline. That diagnosis is therefore unlikely.

The history certainly does not suggest an intrinsic bowel lesion, such as intestinal obstruction. The bowel movements were normal up to the day of admission, and the pains were not typical of intestinal obstruction. The x-ray films are quite confusing, because I cannot figure out, if the cecum was dilated to that extent, why there were no symptoms of obstruction. There was probably subacute obstruction.

Cyst of the omentum, which is a rare lesion, is another possibility, but it would not account for the x-ray findings.

I am inclined to believe that a mesenteric cyst fits the picture better than any other single diagnosis. The symptoms persisted for a long time, and mesenteric cyst, of course, grows to large proportions. To be sure, such a lesion is usually not confined to the right side, but adhesions from the previous operation could have prevented the tumor mass from extending over to the left side and could also explain the enlargement. Bleeding into the cyst would account for the increase in the size of the cyst a few days before entry. I cannot make a positive diagnosis, but my guess is that this woman had a mesenteric cyst possibly causing partial obstruction.

DR. LINGLEY: Was the mass hard or soft?

DR. GIDDINGS: It was fairly firm, it appeared in part to be tympanitic.

DR. LINGLEY: I wonder if the mass felt three years previously could possibly have been the cecum—an anatomic variation of the cecum that had become twisted.

DR. BENJAMIN CASTLEMAN: Do you mean a volvulus of the cecum?

DR. LINGLEY: Yes.

DR. CASTLEMAN: Dr. Giddings, would you give us your impression of the case?

DR. GIDDINGS: We were as confused as Dr. Balch. We knew that the ovaries and the appendix had been removed. We entertained many of the diagnoses that Dr. Balch has mentioned, namely, mesenteric cyst, retroperitoneal cyst and tumor. On the basis of the x-ray evidence we were led to favor a diagnosis of volvulus of either the sigmoid or the cecum.

CLINICAL DIAGNOSIS

Volvulus of sigmoid or cecum

DR. BALCH'S DIAGNOSIS

Mesenteric cyst

ANATOMICAL DIAGNOSES

Acute and chronic cholecystitis, with hydrops, producing partial obstruction of cecum
Cholelithiasis

PATHOLOGICAL DISCUSSION

DR. GIDDINGS: At operation the diagnosis was immediately apparent. In the abdomen an enormously distended gall bladder, 18 cm long and 10 to 13 cm in diameter, extending to the crest of the ilium, was found. It was acutely inflamed and markedly thickened, and there was an adhesion between the gall bladder and the cecum, with apparently partial obstruction and distortion of the cecum to produce the x-ray picture. With removal of the gall bladder the cecum fell back to its normal position.

DR. CASTLEMAN: Can the gall bladder be seen on this film?

DR. LINGLEY: The mass described in the record was probably the gall bladder.

DR. CASTLEMAN: Is it not too low?

DR. GIDDINGS: I think that the mass was a little too far forward on the left for the gall bladder.

DR. CASTLEMAN: The gall bladder we received was enormous, it was fully distended, with marked inflammation, both acute and chronic. A stone impacted in the ampulla had caused the marked distention.

CASE 32352

PRESENTATION OF CASE

A seventy-four-year-old housewife entered the hospital because of abdominal pain.

For two years before entry the patient had had intermittent attacks of sharp periumbilical pain.

An operation was performed on the second hospital day

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The history certainly does not suggest an intrinsic bowel lesion, such as intestinal obstruction. The bowel movements were normal up to the day of admission, and the pains were not typical of intestinal obstruction. The x-ray films are quite confusing, because I cannot figure out, if the cecum was dilated to that extent, why there were no symptoms of obstruction. There was probably subacute obstruction.

Cyst of the omentum, which is a rare lesion, is another possibility, but it would not account for the x-ray findings.

I am inclined to believe that a mesenteric cyst fits the picture better than any other single diagnosis. The symptoms persisted for a long time, and mesenteric cyst, of course, grows to large proportions. To be sure, such a lesion is usually not confined to the right side, but adhesions from the previous operation could have prevented the tumor mass from extending over to the left side and could also explain the enlargement. Bleeding into the cyst would account for the increase in the size of the cyst a few days before entry. I cannot make a positive diagnosis, but my guess is that this woman had a mesenteric cyst possibly causing partial obstruction.

DR. LINGLEY: Was the mass hard or soft?

DR. GIDDINGS: It was fairly firm, it appeared in part to be tympanic.

DR. LINGLEY: I wonder if the mass felt three years previously could possibly have been the cecum — an anatomic variation of the cecum that had become twisted.

DR. BENJAMIN CASTLEMAN: Do you mean a volvulus of the cecum?

DR. LINGLEY: Yes.

DR. CASTLEMAN: Dr. Giddings, would you give us your impression of the case?

DR. GIDDINGS: We were as confused as Dr. Balch. We knew that the ovaries and the appendix had been removed. We entertained many of the diagnoses that Dr. Balch has mentioned, namely, mesenteric cyst, retroperitoneal cyst and tumor. On the basis of the x-ray evidence we were led to favor a diagnosis of volvulus of either the sigmoid or the cecum.

CLINICAL DIAGNOSIS

Volvulus of sigmoid or cecum

DR. BALCH'S DIAGNOSIS

Mesenteric cyst

ANATOMICAL DIAGNOSES

Acute and chronic cholecystitis, with hydrops, producing partial obstruction of cecum
Cholelithiasis

PATHOLOGICAL DISCUSSION

DR. GIDDINGS: At operation the diagnosis was immediately apparent. In the abdomen an enormously distended gall bladder, 18 cm long and 10 to 13 cm in diameter, extending to the crest of the ilium, was found. It was acutely inflamed and markedly thickened, and there was an adhesion between the gall bladder and the cecum, with apparently partial obstruction and distortion of the cecum to produce the x-ray picture. With removal of the gall bladder the cecum fell back to its normal position.

DR. CASTLEMAN: Can the gall bladder be seen on this film?

DR. LINGLEY: The mass described in the record was probably the gall bladder.

DR. CASTLEMAN: Is it not too low?

DR. GIDDINGS: I think that the mass was a little too far forward on the left for the gall bladder.

DR. CASTLEMAN: The gall bladder we received was enormous, it was fully distended, with marked inflammation, both acute and chronic. A stone impacted in the ampulla had caused the marked distention.

CASE 32352

PRESENTATION OF CASE

A seventy-four-year-old housewife entered the hospital because of abdominal pain.

For two years before entry the patient had had intermittent attacks of sharp periumbilical pain

lasting from several hours to several days. Ten days before entry she began to have a particularly severe attack and vomited some whitish material. Because the pain continued she went to bed, where she remained until admission. Seven days before entry she had had several loose bowel movements, but thereafter the stools were brown and normally formed. On the day of admission the patient felt unusually weak, sweaty and nauseated. She vomited several times, producing some whitish material. The periumbilical pain was also severer but was relieved by codeine. When she was seen that night she had been free of pain for about three hours. There had been no hematemesis, melena, fever, chills or upper respiratory infection.

The appendix and one ovary had been removed at the age of twenty-nine.

Physical examination revealed a poorly nourished woman with cold extremities and livid mottling over the chest and abdomen. The pupils were small and reacted poorly to light. The heart sounds were weak but otherwise of good quality. The heart rate was 96. Fine inspiratory rales were heard at both lung bases. The abdomen was soft and non-tender. Peristalsis was somewhat hyperactive. No masses could be felt. Pelvic examination was negative except for a slight prolapse, with cystocele and rectocele.

The temperature was 99°F, and the respirations 18. The pulse and blood pressure were unobtainable.

Examination of the blood revealed a red-cell count of 6,400,000, with 60 per cent hemoglobin, and a white-cell count of 20,000.

The patient was anuric on admission, and no urine was found in the bladder. A small specimen obtained on the following day gave a + test for albumin, and the sediment contained 5 to 10 white cells per high-power field. A culture grew abundant nonhemolytic streptococci. A glove specimen of stool was guaiac negative.

Soon after entry the patient vomited about 150 cc of dark-red material, which gave a ++++ guaiac test. She was given plasma, 5 per cent dextrose in saline and adrenocortical extract. After about three hours of intravenous therapy the blood pressure was 78 systolic, 0 diastolic. A white-cell count done seven hours after entry was 37,400, with 99 per cent neutrophils, and the red-cell count was 6,870,000. Intravenous and intramuscular penicillin was started. Nevertheless the patient gradually lapsed into coma, from which she could be aroused only by painful stimuli.

On the morning after admission the abdomen was noted to be somewhat distended and doughy. Deep pressure in any quadrant caused the patient to cry out. Below the umbilicus in the midline there was a suggestion of a soft mass that did not pulsate. Peristalsis was less active than previously.

Further blood studies revealed a nonprotein nitrogen of 48 mg per 100 cc and a serum amylase

of 50 units. A lumbar puncture and examination of the spinal fluid were negative. A plain film of the abdomen showed gas-filled, dilated loops of small bowel in the midabdomen, which appeared to be jejunum or upper ileum. There was also a considerable quantity of gas in the transverse colon but little distal to the splenic flexure. The loops of small bowel were spread from one another, suggesting the presence of free fluid. A film of the chest was unsatisfactory because of motion but showed a large area of haziness, homogeneous density at the left base.

Toward evening of the second hospital day respirations became gasping in quality. The abdomen had become resistant and was still tender to palpation. A Miller-Abbott tube drained 500 cc of chocolate-brown, guaiac-positive liquid with a fecal odor. Gradually the patient's breathing became progressively shallower, and the blood pressure again fell, despite continuous intravenous fluids.

The patient expired thirty hours after admission.

DIFFERENTIAL DIAGNOSIS

DR EDWARD HAMLIN, JR. May we see the x-ray films?

DR JAMES R. LINGLEY. These films are of rather poor quality but show gas in both the colon and the small bowel.

DR. HAMLIN. Can the gas in the colon be traced from the cecum?

DR LINGLEY. Only around to the region of the splenic flexure, from there on there is extremely little gas. This film of the chest shows a great deal of motion, but there is definite consolidation of the left base.

DR HAMLIN. The one post-mortem finding that I am sure of is bronchopneumonia, but presumably there was something else.

I have been unable, in reading this abstract, to form any satisfactory diagnosis that fits all the criteria. The impression is given that this type of pain existed intermittently for two years, and it becomes difficult to explain this particular attack, which occurred for ten days but with no great change until the very end. The patient had had several loose bowel movements, but the stools were brown and normally formed. Does that mean that she continued to have bowel movements up to entry? I am trying to find out whether there is any question of intestinal obstruction. The question is raised by the x-ray findings to a certain extent, and there are sufficient other factors to make one think of obstruction, although the history is not particularly suggestive. At entry she was obviously in shock. The description of the abdomen is somewhat difficult to interpret, but I gather that the examination was completely negative. Is that correct?

DR DONALD S. KING. This woman was a patient on the Medical Ward on which I was visiting. I

saw her only once on the morning after she was studied in the Emergency Ward. She had entered the hospital in shock, and had been observed by the physicians on various services, including one of the surgical services. At the time I saw her I was told that examination of the abdomen had been absolutely negative on the night of admission.

DR. HAMLIN: She was also obviously dehydrated.

The next thing that interests me is the fact that guaiac-positive material was found in the vomitus but not in the stools, which again implies some degree of obstruction. The white-cell count, which was remarkably high for a seventy-four-year-old woman, despite dehydration, makes one think of infarction. The record on the next morning gives a good description of general peritonitis.

The serum amylase was taken presumably for the question of pancreatitis. In this hospital the serum amylase of 40 units is roughly the top side of normal, so that a serum amylase of 50 is slightly above normal and not particularly helpful.

In summary, this was a disease of relatively long duration that produced an intra-abdominal catastrophe terminally and that caused shock and presumably peritonitis. One might infer that the patient ruptured a hollow viscus and died with, of course, bronchopneumonia. If these assumptions are correct, it might be well to consider the possible hollow viscus that could perforate. The first thing to think of is the bowel, and that brings up the question whether it was the small or large bowel, there are points that lead one to suspect either. The fact that guaiac-positive material was vomited soon after entry makes one believe that possibly this was a relatively high lesion. On the other hand, there is meager x-ray evidence in that direction, and I am unable to call this purely intestinal obstruction, since a negative abdominal examination is unlikely after ten days of obstruction.

Could the gall bladder have perforated? That would explain the long history. Perforation would also explain many of the features and, particularly if it were associated with pancreatitis, could produce shock, but there is nothing in the history to lead one to think of gall-bladder disease in any form. So for lack of corroborative evidence I drop that possibility, which brings me back to the question of bowel.

The obvious lesions that produce a long history such as this patient had are chronic intussusception and chronic volvulus, but they would produce more evidence of obstruction terminally and it is difficult for me to believe that such obstruction was present. I can think of no tumor of the bowel of long duration that causes such a shock-like picture, particularly if the question of blood within the lumen of the bowel is considered, and I have an idea that something is going to turn up to make me feel

extremely embarrassed. That brings us to what seems to me the most probable disease, which fulfills most of the criteria but still leaves something to be desired, namely, mesenteric thrombosis. How it could have occurred intermittently for two years I cannot explain, nor do I think it did, but it explains the essentially normal abdomen on entry and also the rupture of the bowel, as the terminal event.

DR. J. W. EWELL: I should like to raise the possibility of carcinoma of the bowel, with perforation.

DR. HAMLIN: I tried to bring in tumor of varying sorts, but I find myself unable to explain how a tumor could have caused shock without peritonitis.

DR. KING: That also bothered me. When I saw the patient she was practically unconscious. We went over the list of possible causes of shock supposedly from an abdominal condition, and put mesenteric thrombosis high on the list. My own guess, which was wrong, was acute pancreatitis, but the trouble with that diagnosis was that it did not explain satisfactorily the symptoms of two years' duration. It is true that when I examined the patient I did not believe that the abdomen was normal. There was some distention, and even though she was almost in coma there seemed to be some tenderness.

CLINICAL DIAGNOSIS

Acute pancreatitis

DR. HAMLIN'S DIAGNOSES

Mesenteric thrombosis

Bronchopneumonia

ANATOMICAL DIAGNOSES

Strangulated small intestine due to an adhesive band

Hiatus hernia

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The abdomen contained 500 cc of hemorrhagic fluid, and an adhesive band, about 1 cm thick, extended from the under surface of the laparotomy scar to a loop of terminal ileum about 6 cm proximal to the ileocecal valve. Almost the entire ileum, which was gangrenous, was strangulated by this band.

The lesion in the left lower-lung field was not bronchopneumonia. It was a hiatus hernia containing a part of the stomach and intestines and causing collapse of the left lower lobe.

DR. HAMLIN: This case serves again to point out that intestinal obstruction, even without strangulation, does not always present the classic signs and symptoms.

lasting from several hours to several days. Ten days before entry she began to have a particularly severe attack and vomited some whitish material. Because the pain continued she went to bed, where she remained until admission. Seven days before entry she had had several loose bowel movements, but thereafter the stools were brown and normally formed. On the day of admission the patient felt unusually weak, sweaty and nauseated. She vomited several times, producing some whitish material. The periumbilical pain was also severer but was relieved by codeine. When she was seen that night she had been free of pain for about three hours. There had been no hematemesis, melena, fever, chills or upper respiratory infection.

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political education is allowed to come their way
meanwhile Democracy must stand its ground It
as paid too much for what it has won to give up
ny of its ideals

BE NOT THE FIRST

THE physician who has under his care a patient
with Hodgkin's disease, leukemia or some allied dis-
order is not infrequently confronted with the diffi-
cult task of persuading the family, in its despera-
tion, not to cast about for some alleged cure of the
disease rather than to adhere to the more conven-
tional forms of therapy proved by experience to be
beneficial This desire on the part of the family is
easy to understand, for, on the one hand, the phy-
sician in charge must, of necessity, point out the
almost certain fatal outcome, and on the other, the
layman is quick to grasp at straws and all too ready
to believe rumors of true cures by some new and
mysterious substance This is particularly true
when the patient has relatives who are scientists
yet not physicians The situation is made even
more difficult when the lay press publishes premature
and distorted accounts of purely experimental
measures or when a physician, in an unguarded
moment, speaks of a cure when, in actuality, he is
referring to a therapeutic measure under trial that,
at the moment, appears to offer some promise

Twice within the past year the writer of this
editorial has been told by medical students that a
cure for one or another of these malignant or pseudo-
malignant conditions has been found Similar word
has also come to the ears of families some member
of which has been stricken with one of these dread
diseases Thus is false hope raised that serves only
to heighten the distress when failure eventually be-
comes apparent It is probably safe to say that any
doctor thoroughly familiar with these conditions is
aware of what experimental work is being carried
out, and it is also probably safe to say that once a
true cure has been found or a real therapeutic ad-
vance has been made by competent observers this
knowledge will not be long in reaching those in-
terested in the field and, indeed, the medical public
at large Concise official statements from com-
petent investigators may be expected as soon as
they are justified

Such a statement has recently been made by
Rhoads¹ regarding the use of the nitrogen mustards
in leukemia, Hodgkin's disease and certain types of
cancer From this report it is clear that both the
"bis" and the "tris" compounds have definite thera-
peutic limitations and that, broadly speaking, these
substances do not constitute a cure or even a great
advance over the more conventional x-ray treat-
ment Toxic effects, including leukopenia, anemia and
bleeding tendencies, were encountered, and in some
cases the hematopoietic injury exceeded the effect on
the tumor Such remissions as were achieved seldom
lasted more than several months Lymphosarcoma
did not respond to these agents any better than it
does to x-ray, and acute leukemia was not bene-
fited It is stated that chronic leukemia is still
best handled by appropriate radiation, and early,
localized tumors, by radical excision or local radia-
tion It is concluded that "the experimental use of
the nitrogen mustards in the treatment of any active,
extensive, neoplastic process is probably justified
if other methods of control have proved to be with-
out benefit "

In a somewhat similar vein there is a report from
England on the use of urethane in leukemia² Thirty-
two cases were treated, and in most there was a
marked drop in the white-cell count, a reversal of
the differential to more nearly normal and a rise of
the red-cell count, but again the beneficial results
were temporary and there were toxic manifestations
The authors conclude that there is "no indication
that permanent benefit may result from the use of
urethane in either myeloid or lymphatic leukemia "

These reports are not encouraging, but they are
extremely valuable, since they place in the hands of
the attending physician the knowledge that the
conventional form of therapy, whether it be radiation
or surgery or both, is still best in the hands of com-
petent men, and since they form a firm basis on
which to base a reluctance or even a refusal to per-
mit such therapeutic measures to be used in the
average case of neoplastic or pseudoneoplastic
disease

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POSTWAR WORLD

THE postwar world, to date, has been a world of mutual distrust, jealousy and suspicion. It has been a world of unrest, of strife, of disharmony, of violence, of muscle-bulging. We are learning again, as we have learned before and forgotten, that alliance in a common cause does not mean even temporary friendship. The emotional factor of good will is a personal, not a group, phenomenon, and rarely is the moral discipline of the individual sufficient to place good will above immediate self-interest.

The Four Freedoms, around which the allied nations rallied in the dark war days, have been kicked into a cocked hat by some of their adherents and allowed to remain there by the rest. Poland is again bringing to perfection her peculiar art of the pogrom

Mikhailovitch, whom many still suspect of having been one of Yugoslavia's great patriots, has been eliminated by due process of postwar law, on the other hand Bolivia's dictator, after a man hunt through his palace, was recently liquidated and hanged *in corpore delicti*.

Palestine, which gave us one of our early examples of man's violent reactions to a policy of good will toward man, still furnishes us with illustrations of violent reactions. Trieste, that gem of the Adriatic, is again the victim of a snatching contest. China is being spun like a top by her various factions, and Madame Sun Yat-sen, perhaps with some justice, wants the Americans out. Manchuria has apparently been thoroughly looted by our hearty former co-belligerents, the genial Russians, of whom it is currently said, however, that the marshals who won the war are being looked on coldly by the big boss.

Nature has done her best to add to mankind's confusion by providing two years of almost unprecedented crop failures over much of the world, and economic unrest at home seems to be accompanied by that strawberry shortcake of modern journalism—an outbreak of private slaughter, mayhem and rape. Congress, moreover, according to present indications, seems of a mind to preserve the Nation's health by right of eminent domain.

Our domestic problems we will no doubt stagger along with and settle in the usual bivalent democratic fashion—partly right and partly wrong. So far as our foreign relations are concerned, Brooks Atkinson, the able *New York Times* correspondent recently returned from Russia, has given probably the best picture of the working policy toward its neighbors of the bear that walks erect. It might be phrased in the words of the mate of the whaler *Mozambique* to his skipper: "All I wants from you is ceevility and d— little of that!"

We now know that Russia is bent on fulfilling her own destiny and believes that destiny to be incompatible with the rights of other nations. Her government has not learned—perhaps cannot learn—the lesson of compromise and cannot understand that various political ideologies may exist side by side in the same world. Much may be expected eventually of the Russian people, when

the body only which is out of health, but always the complete being." Often the reasons for leaving the hospital are obscure and great skill is needed to help the patient to be realistic and to direct himself toward the goal of complete recovery.

The treatment and hospitalization of patients with tuberculosis involves months or years of restricted activity. A young athletic boy, suddenly faced with tuberculosis, may revolt at accepting this state. Since the tubercle bacilli carry on their destructive work insidiously, the patient, after he has regained some strength, will insist that his cure is completed. This view is maintained despite the contrary evidence of x-ray and sputum reports. Perhaps the fear of the disease is so great as to cause the patient to reject its reality.

The older man and woman, accustomed to years of labor in factory and home, may also find it difficult to accept the new role of inactivity and dependency. Experience has not fitted them to fill the passing empty hours. The thought of lying quietly in bed while the world hurries on is untenable, and they are tortured by the desire to be back among the working multitudes.

This boredom is more readily conquered by patients accustomed to study or reading, or those who are fortunate enough to have a hobby. Hospitalization is a difficult experience for the majority, but it can be a constructive one. Rarely does a patient who has found activities that lead to growth and development, sign out against advice. There is also a distinct difference between those patients who have made their adjustment and those who have succumbed to the sheltered life of the hospital and have regressed to an infantile, dependent level.

There does not appear to be any constant point at which a patient may feel that the hospital is no longer bearable. Even when he may be apparently adjusted to the hospital routine, the inactivity may lead to cumulative effects until a breaking point is reached. A little supportive treatment at this time will often tide the patient over the rough spot.

A patient entering a hospital brings with him the sum total of his life experiences. He has certain ties, certain obligations, and these remain though they are altered by the new experience. Early contact with the patient and his family can give clues to the patient's motivations and the part the family will play. The marital strengths, the interfamily ties and strains, the relationship in a changing setting should all be weighed and evaluated with the patient. The patient must, if possible, be spared the worry and anxiety of the family. This cannot be done by simply hiding or ignoring real problems. If the family is aware of this, they can show the patient their strengths in meeting problems and assure him that they can keep their balance.

The social worker is often faced with a recently admitted patient who demands to leave the hospital with or without the doctor's permission. An interview usually begins with the patient demanding, "How can I remain here while my family starves?" The social worker can be of invaluable aid in directing the family to sources of help and thus make it possible for the patient to accept his hospital stay knowing that his family will not starve or go homeless.

Life in a hospital is complex. A patient is faced with the need to adjust to his companions, the doctors, the nurses and other personnel. He has to give up practically all his privacy, both physical and mental. There are new ideas to be adjusted to in this microcosm of all nations and races. It is not difficult for friction to arise between the patient and a particular person or routine. Personalities may clash and the sick person may feel that the only solution lies in leaving the hospital. Sometimes the patient does not indicate the real reason for signing out but gives the usual statement that he "can do just as well at home." Other patients are quite verbose regarding the sources of annoyance.

All members of the hospital team can play very important parts in helping the patient adjust not only to his illness but to the hospital life. A healthy adjustment in the hospital implies a psychologic awareness and acceptance of the illness. When the acceptance has not been achieved, the patient rejects the hospital as a symbol of the disease. In the adjustment of the patient to the hospital one factor that might be given special attention is the food. Tuberculous patients are very conscious of the role of food in their cure and of the variations in their weight. This is one of the chief topics of conversation. One director of a sanatorium when asked how he kept down his A O R discharges to a surprisingly low figure

replied that he gave the patients the type of food they would get in their own homes.

An analysis cannot give all the reasons why patients interrupt the treatment process. The individuality of every situation is marked, and therein lies the challenge. The problem is a big one. There has been a constant war against tuberculosis. In its earlier stages this fight was on a mechanical level of cleaning up slums, taking mass x-rays or providing the proper type of hospital care. But now we have come to realize that we are dealing with human beings and the control of the disease will come only when the sick person is prepared to participate. — Reprinted from *Tuberculosis Abstracts*, August, 1946

CORRESPONDENCE

CESAREAN SECTION VERSUS TEST OF LABOR

To the Editor: In his paper appearing in the June 27 issue of the *Journal Dr Waters*, in discussing fetopelvic disproportion in the borderline pelvis, states "We frankly admit our inability in many such cases to decide in advance of an adequate test of labor the ability of the patient to deliver herself or to be safely delivered by vagina. We marvel at the judgment and experience of the omniscient, which permit in advance of labor appreciation of the size, shape and moldability of the fetal head, the extent of the physiological relaxation of the pelvic joints, the thickness and tension of the nonosseous pelvic structures, the character and effectiveness of the uterine contractions, the time factor in even partial dilatation and effacement of the cervix." This represents at once an admirable candor and a great waste of wonder. It poses numerous questions.

What is obvious fetopelvic disproportion? Is it invariably concomitant with contracted pelvis borderline or otherwise? What is an "adequate test of labor"? Who are those who possess such judgment and experience that in advance of labor they appreciate the factors listed by Dr Waters? Where does he find the names or writings of those termed "omniscient"? When and where have they stated that they possess in advance of labor the fundamental obstetric information suggested by Dr Waters? Will he tear away the veil of anonymity?

It is no omniscience which we bring to our opposition to test or trial of labor. It is rather a profoundly felt resentment of our own ignorance coupled with the fact that we have learned that an adequate test of labor is no cheap commodity. It has no fixed or predictable price. All too often obstetricians are faced with the problem posed by Dr Waters. All too often, despite all available data, including accurate clinical and x-ray mensuration and the excellent procedure of Hillis, we do not know in advance of labor whether or not the presenting vertex will enter the pelvis. Faced with our own ignorance we have available for the solution of the problem two procedures each necessarily a mere reflection of that ignorance. One may proceed to elective section or to adequate test of labor. Our choice is elective section because we know what it costs.

What is the price of section? The mortality for elective section of the lower segment type is 0.5 per cent.

What exacton is made for a test of labor? Perhaps none. Perhaps twenty-four to ninety-six hours of irregular, purposeless, inefficient pain with the patient undelivered, exhausted and infected at the end of such time — a major surgical risk. Perhaps a long labor with a badly battered or dead baby as a reward. Perhaps a long labor terminated by a technically and physically difficult instrumental delivery with injury or death to the baby and the mother left with a vesical or rectal fistula or a permanently relaxed or damaged pelvic floor. Perhaps death. There is no fixed or predictable price.

In the day when mortality following section was 50 per cent test of labor was mandatory and section barely thinkable. That day passed in 1882. Test of labor should have passed with it. It properly belongs with the thinking of 1882.

There is no omniscience in electing section. There is knowledge of the cost and knowledge of the outcome. Section electively performed carries a mortality of 0.5 per cent, and section thus performed will increase section incidence by 1.5 to 2.0 per cent.

In the matter of management of the patients exhibiting eclampsia, Dr Waters states, "We do not perform cesarean

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BUSSEY — Floyd H. Bussey, M.D., of New Bedford, died May 1. He was in his sixty-second year.

Dr. Bussey received his degree from the University of Michigan Homeopathic Medical School in 1910. He was a fellow of the American Medical Association.

COLLINS — Richard Collins, M.D., of Waltham, died July 28. He was in his seventy-second year.

Dr. Collins received his degree from Harvard Medical School in 1900. He was a member of the staff of the Waltham Hospital, a member of the American College of Surgeons and a fellow of the American Medical Association.

His widow, a son and a daughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

POSTPONEMENT OF ELECTIVE TONSILLECTOMY

The Department of Public Health again feels it necessary to advise against elective tonsillectomy during the poliomyelitis season. This constitutes one of the few effective measures that can be taken to minimize the serious effects of poliomyelitis. Although the incidence of the disease is not so high this summer as it was last year, cases are occurring regularly and it is significant that a history of antecedent tonsillectomy was given in three cases, two of which had bulbar paralysis.

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1946

RÉSUMÉ

DISEASES	JULY 1946	JULY 1945	SEVEN YEAR MEDIAN
Anterior poliomyelitis	11	33	5
Chancroid	2	2	*
Chicken pox	516	363	400
Diphtheria	34	13	13
Dog bite	1372	1229	1227
Dysentery, bacillary	5	44	23
German measles	134	62	62
Gonorrhea	447	537	356
Granuloma inguinale	1	1	*
Lymphogranuloma venereum	2	4	*
Malaria	39	136	1
Measles	2533	735	1159
Meningitis, meningococcal	4	13	13
Meningitis, Pfeiffer bacillus	1	2	2
Meningitis, pneumococcal	7	3	3†
Meningitis, streptococcal	0	0	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	0	1	2†
Meningitis, undetermined	7	0	4†
Mumps	216	686	434
Pneumonia, lobar	70	112	112
Salmonella infections	14	8	9
Scarlet fever	183	263	241
Syphilis	486	321	388
Tuberculosis, pulmonary	278	275	255
Tuberculosis, other forms	13	11	18
Typhoid fever	7	0	4
Undulant fever	10	3	4
Whooping cough	564	587	521

*Made reportable December 1943

†Four-year average.

COMMENT

Diseases reported at an incidence above the seven-year median included chicken pox, German measles, measles, typhoid fever and whooping cough.

Although anterior poliomyelitis was reported at a figure above the median prevalence, there is no evidence at present that this disease will reach epidemic proportions this year.

Diphtheria was reported at the highest figure for the month of July in the past ten years. This was also true for the months of May and June.

Diseases reported below the median prevalence included bacillary dysentery, meningococcal meningitis, mumps and scarlet fever.

Lobar pneumonia was again at a record low for the sixth consecutive month.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Arlington, 2; Boston, 1; Cambridge, 1; Falmouth, 1; Marblehead, 1; Medford, 1; Washington, 4, total, 11.

Diphtheria was reported from Boston, 6; Cambridge, 1; Chelmsford, 1; Everett, 1; Framingham, 2; Gloucester, 1; Lowell, 2; Lynn, 1; Newton, 2; Somerville, 2; Taunton, 6; Worcester, 3, total, 34.

Dysentery, bacillary, was reported from Boston, 1; Worcester, 4, total, 5.

Encephalitis, infectious, was reported from Southbridge, 1, total, 1.

Malaria was reported from Arlington, 1; Attleboro, 1; Boston, 14; Bourne, 1; Cambridge, 2; Georgetown, 1; Haverhill, 2; Hingham, 1; Longmeadow, 1; Lynn, 2; Medford, 1; Newton, 1; North Andover, 1; Peabody, 1; Rockport, 1; Salem, 1; Shrewsbury, 1; Townsend, 1; Waltham, 1; Winchester, 1; Worcester, 3, total, 39.

Meningitis, meningococcal, was reported from Boston, 2; Fitchburg, 1; Holyoke, 1, total, 4.

Meningitis, Pfeiffer bacillus, was reported from Boston, 2, total, 2.

Meningitis, pneumococcal, was reported from Amherst, 1; Belmont, 1; Boston, 3; Fitchburg, 1; Malden, 1, total, 7.

Meningitis, undetermined, was reported from Brookline, 2; Cambridge, 1; Millbury, 1; Newton, 1; Plymouth, 1; Worcester, 1, total, 7.

Salmonella infections were reported from Belmont, 1; Bernardston, 1; Boylston, 1; Cambridge, 1; Falmouth, 1; Lawrence, 2; Lowell, 1; Newburyport, 1; Newton, 1; Northampton, 1; Templeton, 1; Waltham, 1; Worcester, 1, total, 14.

Septic sore throat was reported from Boston, 5; Foxboro, 1; Greenfield, 1; Quincy, 1, total, 8.

Trichinosis was reported from Boston, 1; Cambridge, 2, total, 3.

Typhoid fever was reported from Andover, 1; Arlington, 1; Boston, 1; Chelsea, 1; Somerville, 1; Springfield, 1; Worcester, 1, total, 7.

Undulant fever was reported from Adams, 2; Carlisle, 1; Dalton, 1; E. Bridgewater, 1; Groveland, 1; Hinsdale, 1; Taunton, 1; Templeton, 1; West Springfield, 1; Westfield, 1; Worcester, 1, total, 12.

MISCELLANY

THE SIGNING OUT OF TUBERCULOUS PATIENTS

When the private physician makes a diagnosis of tuberculosis and succeeds in getting a patient under sanatorium care, he is apt to feel that his job is done. If that patient leaves the sanatorium prematurely, his physician will be handicapped in his subsequent efforts by the failure of this first hospital experience. A knowledge of some of the factors that lead tuberculous patients to leave hospitals against medical advice should help physicians to prepare patients for accepting and completing hospital care. The matter is discussed in a paper, "The Signing Out of Tuberculous Patients," by Jean Berman and Leo H. Berman, which appeared in the April, 1944, issue of *The Family*.

Those who are interested in helping a patient to use the medical care necessary for recovery and to accept a possible physical limitation, find challenging problems in work with the tuberculous. The importance of this may be realized when hospitals in different parts of the country report that from 22 to 65 per cent of their patients leave A. O. R. ("at own risk").

The patients who refuse all treatment have not been considered. The focus has been on patients who have evinced a desire to get well but who during the course of treatment attempted to terminate their recovery process. All hospital personnel, including the social worker, must accept "It is never

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PULMONARY TUBERCULOSIS IN HARVARD MEDICAL STUDENTS*

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BOSTON

DESPITE the marked fall in recent years in the morbidity and mortality due to pulmonary tuberculosis and despite advances in its early diagnosis and treatment, tuberculous infection of the lung remains the most serious medical problem that confronts the medical student. Although for more than a century European clinicians had been aware of an apparent high incidence of pulmonary tuberculosis among medical students, it was not until 1930 that Steidl¹ called to the attention of American clinicians the fact that a similar high incidence was being overlooked in American medical schools. Stimulated by Steidl's report, Hetherington and his co-workers² conducted a survey showing that over 20 per cent of the senior class at the University of Pennsylvania Medical School had what they considered to be significant adult-type pulmonary tuberculosis. This alarming report stimulated the undertaking of surveys at other medical schools. In 1939 Soper and Amberson³ reviewed information collected from surveys made at the medical schools of the universities of Pennsylvania, Wisconsin and Oslo and of Johns Hopkins, Yale, Columbia, Harvard, Stanford and New York universities and at the Woman's Medical College. The incidence reported from these schools varied from 0.4 per cent (Columbia) to 13.5 per cent (University of Pennsylvania). Since Soper and Amberson's report surveys have been conducted at Cornell⁴, Northwestern⁵ and New York universities.⁶

As might be expected, there was significant variation in the rates at various schools, depending on the geographical origin of the student body, the location of the school, the diagnostic criteria and the care with which the survey was conducted.

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Many schools, particularly in the early reports, found that the previously known incidence tripled or quadrupled when formal case-detecting programs were instituted. Other factors, such as the irregular occurrence of epidemics of tuberculosis in certain highly susceptible or heavily exposed classes, occasionally operated to produce unduly high figures. Furthermore, some of the high incidences reported in the earlier papers appear to be partly based on the presence of lesions that would now be considered obsolete tuberculosis of no clinical importance. It was presumably a combination of many such factors that produced the uniquely high figures at the University of Pennsylvania—a rate rarely even approached in the experience of other schools. Most carefully conducted surveys report an incidence in the neighborhood of 1 or 2 per cent.

In the light of present knowledge, it is the purpose of this paper to review and analyze the material on pulmonary tuberculosis that has accumulated in the records of the health office at Harvard Medical School during the last twenty-three years. In so doing an endeavor will be made to trace the steps that led to the evolution of the case-finding program now employed at Harvard Medical School.

MATERIAL AND METHODS

The data presented in this study were obtained chiefly from a search of the records kept by the physicians to students at Harvard Medical School. The medical histories of twenty-four classes, beginning with the class of 1926, were studied. All available clinical information in the files of the Health Office, as well as sanatorium reports and personal communications, was reviewed in each case. The x-ray films available in 23 cases were reviewed, with special attention to the extent and location of the lesions.

In all cases presented in this study chest films showed either the appearance of a lesion not previously present or extension of a previously known

§These records were kept by Drs. Reginald Fitz, Clark Heath, Eugene Eppinger, Lewis Dexter and Lewis Kane.

section on patients with eclampsia unless antitoxic measures have checked the eclampsia and made the patient operable." Now how is it known that the "antitoxic measures" have checked the eclampsia? How is it known that the patient has been made "operable"? What are the measures which have such virtue? If a convulsion is stopped medically has the eclampsia ceased? If measures stop convulsions, how predict the time at which the next will arrive? How long does Dr. Waters wait after eclampsia is checked before he operates? What criteria does he use to determine the operability of the patient?

Dr. Waters is to be congratulated on the excellent record of his clinic. His paper is of great value and certainly contains a wealth of provocative and stimulating matter.

MILTON J. SCHREIBER, M.D.

320 Central Park West
New York 25, New York

* * *

Dr. Schreiber's letter was referred to Dr. Waters, whose reply is as follows:

August 6, 1946

To the Editor: The wording of the referred-to paragraph is sufficiently explicit, I trust, even to the omniscient, to clarify our attitude with respect to test of labor. Dr. Schreiber determines *in advance of labor*, after considering "all available data including accurate clinical and x-ray mensuration and the excellent procedure of Hillis" whether or not a patient requires a cesarean section. Since none of us may possess the fundamental obstetric data which I referred to but which all of us, including Dr. Schreiber, must at least consider, it is clear that he qualifies most excellently as one of the "omniscient" and can find his companions in the literature with no help from me.

The picture Dr. Schreiber paints of the patient who has been given a test of labor is harrowing and pitiful, even though nonexistent, at least in our clinic. With adequate analgesia, supportive ante-partum therapy and careful labor observation, there is no reason why such patients should be exhausted, dehydrated, infected or poor surgical risks. If a gross error of judgment is made, which on occasion seems well within our experience, there are suitable operative procedures which minimize the risk and approximate the mortality given by Dr. Schreiber for purely elective section.

In my own private service I have had no maternal cesarean death in more than fifteen years following any type of cesarean operation. With rare exceptions, I invariably allow primiparas enough labor to demonstrate the effectiveness of the normal mechanism, and if the hours of labor and ruptured membranes exceed our safety period, I resort to extra-peritoneal section—which even then is as safe as the elective operation. To me, a test of labor so conducted is a cheaper "commodity" than increasing the general cesarean incidence by 1.5 to 2.0 per cent, and I question the quoted 0.5 per cent mortality for elective cesarean section if applied to the country at large.

I trust those who read Dr. Schreiber's letter will also read my article and study the tabular data given on eclampsia, which should satisfy the questions asked. Most patients who have eclampsia will deliver vaginally. But an independent indication for section may be present, or the patient may fail to maintain improvement after a seeming happy response to initial therapy. Cessation of convulsions, recovery from coma and stupor, clearing of the pulmonary passages, lowering of blood pressure and pulse rate, and restored urinary output will serve notice that operation may be assayed under spinal anesthesia in the needed case, but with an accepted risk by virtue of the eclamptogenic toxemia itself. Experience with enough clinic and post-mortem material teaches that no didactic answers may be made to Dr. Schreiber's questions on eclampsia. We are guided to such answers by the considered results of experience over years as applied to each eclamptic patient, and the efficacy of our scientific guessing or balanced judgment as you will may be determined from the data I submitted. That, I believe, speaks sufficiently well for itself.

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BOOK REVIEW

A Manual of Surgical Anatomy By Tom Jones and W. C. Shepard. Prepared under the auspices of the Committee on Surgery, Division of Medical Sciences, National Research Council. 4th ed., cloth, 195 pp., illustrated. Philadelphia and London: W. B. Saunders Company, 1945. \$5.00.

This excellent manual measures up to the high purpose for which it was developed. In the words of Major General Norman T. Kirk, the surgeon general of the Army, the aim of the manual is "to provide a concise atlas of applied surgical anatomy which permits rapid visual review of any part of the body and the proper surgical approaches to the various regions to the surgeon who may be called upon to perform urgent surgical procedures on the wounded." The drawings, arranged regionally, are from the skillful hands of the expert artists Jones and Shepard. The illustrations are simple line drawings, with the names placed on the various structures themselves. Inasmuch as good surgery depends, to a large extent, on thorough familiarity with the anatomy and structural relation of the parts involved, a careful thoughtful study of the illustrations will serve the best interests of the surgeon. There is a useful fifty-four-page explanatory index. The text is divided into four parts: head and neck, trunk-thorax, abdomen and pelvis, upper extremity, and lower extremity. This book makes a definite contribution to medical and surgical thought and merits a wide reception.

NOTICES

DIABETES CLINIC

Eli Lilly and Company will sponsor a diabetic clinic to be held at the Indiana University Medical Center in Herty Hall of the State Board of Health Building, Indianapolis, Indiana, on September 23—a week following a program at the University of Toronto in honor of the twenty-fifth anniversary of the discovery of insulin. International importance will be given to this meeting by the presence of Professor Charles H. Best, of Toronto, Canada, Professor Bernardo A. Houssay, of Buenos Aires, Argentina, Dr. R. O. Lawrence, of London, England, and Dr. H. C. Hagedorn, of Gentofte, Denmark. Various phases of diabetic care will be discussed.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 5

TUESDAY, SEPTEMBER 10

12:00 m–1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater, Dowling Building, Boston City Hospital.
*12:15–1:15 p.m. Clinicooncogenetological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, SEPTEMBER 11

*10:30–11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Childreo Hospital.
*12:00 m. Clinico-pathological Conference (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital.
*2:30–4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Childreo Hospital.

*Open to the medical profession.

MARCH 15–SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240 issue of February 14.

SEPTEMBER 4–7. American Congress of Physical Medicine. Page 616 issue of May 2.

SEPTEMBER 5. New England Hospital for Women and Children. Page 284 issue of August 22.

SEPTEMBER 12. Brochietasis and Pulmonary Abscess. Diagnosis and treatment. Dr. Maurice Segal. Pentucket Association of Physicians. 5:30 p.m. Haverhill.

SEPTEMBER 16–18. American Diabetes Association. Page 284, issue of August 22.

SEPTEMBER 23. Diabetes Clinic. Notice above.
SEPTEMBER 30–OCTOBER 2. Congress on Industrial Health. Page 254 issue of August 22.

OCTOBER 6–12. Interamerican Congress of Cardiology. Page 211, issue of June 6.

OCTOBER 7–12. Seminar in Legal Medicine. Page 206 issue of August 2.

(Notices continued on page 3111)

The demonstration of an incidence almost three times that known before the introduction of a case-finding program is in accord with the experience of other medical schools. At the universities of Minnesota,¹¹ Wisconsin¹² and Pennsylvania² and at Yale University¹³ the introduction of case-finding programs increased the previously known rate between four and six times.

Development of Tuberculosis according to Academic Year

The academic year in which the lesion was first discovered is known in 34 of the 44 cases and is listed in Table 2. The fourfold increase in the

TABLE 2 Cases of Tuberculosis according to Academic Year of Appearance

YEAR OF APPEARANCE	NO OF CASES
On entrance	3
First	1
Second	3
Third	11
Fourth	12
Total	34

number of cases appearing in the last two academic years, as compared with the first two, is discussed below. A similar finding has been reported from other medical schools.^{2, 5, 6, 14}

Significance of Tuberculin Reaction

The tuberculin reaction on entrance to medical school was known in 26 cases prior to the development of the pulmonary lesion. Sixteen students were positive reactors, and 10 were nonreactors. Of the former, 3 were found to have active lesions on x-ray examination at entrance, 13 positive reactors and 10 nonreactors developed lesions during medical school. Since Classes 1936 to 1948 included 51.7 per cent positive reactors and 48.3 per cent nonreactors on entrance, the ratio of 13 positive reactors to 10 nonreactors suggests that the nature of the tuberculin reaction on entry had little influence on the development of active pulmonary tuberculosis in medical school.

On the other hand, conversion from nonreactive to reactive state while in medical school carried a definite liability. In Classes 1936 to 1947 there were 188 students who were nonreactors on entrance but who subsequently became reactors while in medical school. Of these, 10 (5.3 per cent) developed active pulmonary tuberculosis in medical school, and at least 3 others developed parenchymal or pleural tuberculosis soon after graduation. Information on the status of the remainder of the group after graduation is too fragmentary to permit estimation of a postgraduate incidence.

Three students who developed clinical pulmonary tuberculosis were known to have been nonreactors five, eleven and eleven months before the diagnosis was established. The importance of this fact in determining the proper timing of the interval when routine x-ray examination or tuberculin tests should be performed is discussed below.

No case of pulmonary tuberculosis was found in any student with a negative tuberculin reaction. The number of positive reactors, if any, who became nonreactors during medical school is unknown, since positive reactors were not retested. In non-medical groups it has been shown that a small but significant number of reactors lose their reactive state during varying periods of observation.^{15, 16}

Classification of Pulmonary Lesions

The extent and intensity of the pulmonary lesions were classifiable in 26 of the 31 cases in classes 1936 to 1948. On the basis of the National Tuberculosis Association criteria,¹⁰ 18 were minimal lesions, and 8 were moderately advanced. Cavitation was rare, being demonstrable in only 3 cases.

Since most of the lesions were minimal all were subgrouped according to the classification of Sampson¹⁷ in use at the Trudeau Sanatorium, which is based on intensity (chiefly density) of the lesion, as well as on its area. Intensity A is slight, B is

TABLE 3 Disability according to Severity of Lesion

CHARACTER OF LESION	TOTAL NO OF CASES	NO OF CASES NEEDING SANATORIUM CARE	AVERAGE SANATORIUM STAY	NO WITHDRAWING FROM MEDICAL SCHOOL
Minor	13	6	14	1*
Major	13	11	30	3

*Because this student had diabetes mellitus and active pulmonary tuberculosis on entry, he was advised to withdraw.

moderate, and C represents consolidation, cavity or dense fibrosis. Any of these intensities may be applied to a minimal, moderately advanced or far advanced lesion. When the 26 cases were so reclassified, 13 appeared as minimal of A intensity and constituted the minor-lesion group. Thirteen others appeared as minimal of B or C intensity or as moderately advanced of A, B or C intensity, constituting the major-lesion group. Pleural effusions were classified as major lesions.

Confirming the validity and prognostic value of this grouping was the marked difference in degree and duration of disability between the categories. Of the 13 cases comprising the minor-lesion group, 7 students did not require sanatorium care. For the 6 requiring sanatorium care, the period of hospitalization varied from ten to twenty months, with an average of fourteen months. Two of these

lesion. Calcified primary complexes, however extensive, thickened apical caps, blunted costophrenic angles and small apparently obsolete nodules were not considered clinically significant, and are not included in any of the tabulations or discussions. Supporting clinical evidence for activity included at least one of the following characteristic symptoms: cough, hemoptysis, fever, anorexia, weight loss and general malaise. In many cases acid-fast bacilli were demonstrated in the sputums, gastric washings or pleural effusions, either by direct observation or by guinea-pig inoculation.

The tuberculin-test figures were derived from the original work sheets of the routine tuberculin surveys. The two-test-dose, intradermal method was used, the results being read in forty-eight hours. Induration of at least 5 mm in diameter was used as the sole criterion of a positive test. No student was considered a nonreactor unless the full strength of the second dose — 10 mg O T (Old Tuberculin) or 0.005 mg P P D (Purified Protein Derivative) — had been given. Classes 1936 through 1940 and the Class of 1941 during its first three years were tested with O T, all subsequent classes were tested with P P D.

From 1922, when records were first kept, until 1932 no routine case-detection program was employed. In the latter part of this period, however, more than four hundred chest x-ray films were taken on the basis of weight loss, history of contact, suggestive symptoms or suspicious signs.⁷ The first routine case-detection program, which was adopted in 1932, consisted of intradermal tuberculin tests and x-ray examination of the chest for all members of the entering classes and also for many members of the graduating classes. In 1936 the plan was extended to include annual tuberculin retesting of all nonreactors, and all positive reactors were encouraged to have annual x-ray examinations of the chest.⁸ The present method was adopted in 1943, although it did not have complete application until 1944. Routine tuberculin tests and x-ray examinations of the chest were done on all members of the entering classes. The students were then re-examined semiannually — tuberculin reactors by x-ray and nonreactors with tuberculin. Although the semiannual rule was not effectively enforced until 1944, its official adoption in the preceding year led to virtually complete participation of the student body in at least one routine examination in that year, participation had previously been wide but not complete.

RESULTS

X-ray Findings

From 1922 through 1945, a total of 44 students were known to have developed active pulmonary tuberculosis on the basis of the criteria outlined above. The x-ray films were available for study in

23 cases, in the remainder the information was gleaned from the reports of the radiologist.* Most of the lesions were in the apical or subclavicular areas. A characteristic position was the outer portion of the second anterior interspace, as pointed out by Sosman.⁹ About 70 per cent were minimal (National Tuberculosis Association classification¹⁰), and the remainder moderately advanced. There were no known far advanced lesions in the initial x-ray films. Demonstrable cavitation was rare, occurring in only 3 cases. Four cases that developed in medical school and had apparently inactive lesions in the x-ray films on admission are included in this study because none of the lesions appeared to be a direct recurrence of a previous one. In 2 cases of massive pleural effusion without demonstrable parenchymal involvement, acid-fast organisms were demonstrable in the pleural fluid.

Incidence

Of 3160 students in Classes 1926 to 1948, it is known that 44 developed pulmonary tuberculosis — an over-all incidence of 1.4 per cent. Because of the relative inefficiency of the case-finding program prior to 1936, however, the actual rate of the disease was undoubtedly considerably greater. Thus Classes 1926 to 1932, in which no organized case-finding program was conducted, had an incidence of 0.9 per cent. Classes 1933 to 1936 had routine chest films and tuberculin tests on admission, and many, but not all, students had chest films in their fourth year, in this group the incidence was 1.1 per cent. These figures may be contrasted with those for Classes 1937 to 1943, in which routine chest x-ray examination and tuberculin tests on admission were followed by annual re-examination of all nonreactors by the tuberculin test and of

TABLE 1 Incidence of Tuberculosis according to Type of Case-Detecting Procedure

CLASSES	PROCEDURE	NO OF STUDENTS*	NO OF CASES	INCIDENCE %
1926-1932	Symptoms and physical examination	893	8	0.9
1933-1936	Entrance tuberculin test and x-ray examination, with (recommended) repetition at graduation	496	6	1.2
1937-1945	Annual tuberculin test and (recommended) x-ray examination of reactors	1153	25	2.2
1946-1948†	Semiannual tuberculin test or x-ray examination	—	5	—

*Corrected for second year and third year transfers.

†These classes have not yet completed medical school.

most positive reactors by x-ray examination, and in which the rate was 2.2 per cent. The apparent variation in incidence, correlated with the type of case-finding program, is given in Table 1.

*All films were originally examined or later reviewed by Dr. Merrill C. Sosman at the Peter Bent Brigham Hospital.

in tuberculosis in the general population. A similar decreasing incidence of positive reactors during approximately the same period has been noted among students entering college¹⁹ and other medical schools.¹⁴

The rate of conversion of nonreactors to reactors while in medical school is shown in Table 9. Except for the third-year and fourth-year tests on Classes

lesions have had prolonged periods of disability, averaging over two and a half years of absence from medical school. In addition, several failed to complete their medical education. Almost without exception, students whose lesions were detected by the appearance of symptoms showed major lesions, whereas just as regularly students whose lesions were detected by routine examination showed minor lesions. Only about half the students with minor lesions required sanatorium care. The average stay of those who required such care was fourteen months.

The demonstrable effectiveness of routine examination in the detection of early lesions makes frequent examination mandatory. The original case-finding program at Harvard Medical School, consisting of routine tuberculin tests and chest x-ray examination on entry and at graduation, has been progressively modified to the present semi-annual examination. During the period of annual examination one of us (H P B²⁰) was able to show, on the basis of the existing Harvard Medical School material, that when routine chest x-ray examinations were done only annually or approximately annually, a large proportion of the lesions became symptomatic, and were thereby detected, before the time of re-examination. In addition, at least 3 students developed major lesions within a year of having been found to be nonreactors in the annual test.

Since major lesions often develop within a year after infection or after a negative chest x-ray examination, it is our belief that six months repre-

TABLE 9 Cumulative Attack Rates of Entrance Nonreactors Who Became Positive Reactors during the Second, Third or Fourth Year*

CLASS	PERCENTAGE
1936	36
1937	47
1938	38
1939	33
1940	41
1941	24
1942	32
1943	27
1944	41
1945	28

*In Classes 1936 to 1939 the rates are based on a single fourth year test of entrance nonreactors. In classes 1940 to 1945 the rates are based on accumulation of reactors in annual and semiannual retests of entrance nonreactors.

sents the maximum interval that should be allowed to elapse between routine x-ray examination of tuberculin reactors and tuberculin tests of non-reactors. When students previously nonreactors become reactors in the semiannual examination, x-ray examination of the chest should probably be done every six weeks for six months, and every three months for the remainder of the year. The use of this case-finding routine examination has, so far, eliminated the previously preponderant major

TABLE 8 Tuberculin Reactions on Entrance

CLASS	NO OF STUDENTS	NO OF STUDENTS TESTED	NO OF REACTORS	PERCENTAGE OF REACTORS
1936	123	120	84	78
1937	125	124	101	81
1938	124	118	78	66
1939	126	122	74	61
1940*	125	124	62	50
1941	125	125	74	59
1942	126	123	52	42
1943	128	128	43	34
1944	127	125	66	53
1945		124	56	45
1946*		123	34	44
1946b		122	40	33
1947		112	45	40
1948		110	50	45
Average				52

*The OT used for this class was subsequently reported to be of substandard potency by Seideman.¹⁸

1944 and 1945, the retests were done in the first two months of each academic year, and the results were therefore largely the effects of the preceding year. Although the significance of the class variation (24 per cent for the Class of 1941 and 47 per cent for the Class of 1937) remains speculative, the high level of these attack rates is noteworthy. If one assumes that the acquisition of the reactive state represents tuberculous infection, approximately 34 per cent of students became infected during medical school.

By means of the annual tuberculin test it was possible to determine an annual attack rate for each class. Although there was considerable variation from class to class, the average attack rates for each academic year showed surprisingly little variation. For the six classes 1940 through 1945, the rates were as follows: second-year test 12 per cent, third-year test 13 per cent, and fourth-year test 13 per cent (Table 10). The relation between this remarkable constancy in attack rate per year and the preponderance of pulmonary tuberculosis in the last two academic years is discussed below.

DISCUSSION

Pulmonary tuberculosis is the most serious medical problem that confronts the health departments of medical schools. Since the institution of an efficient case-finding program, the known incidence at the Harvard Medical School has been 2.2 per cent. Of special importance are cases with more than minor pulmonary lesions. Students with such major

6 are still in sanatoriums — 1 for six months and the other, now about to return to school, for twenty months. On the other hand, of the 13 cases in the major-lesion group, only 2 students did not require sanatorium care. Of the 11 who entered sanatoriums, 3 failed to return to medical school (after five, five and two years). The remaining 8 students spent from one to five years in sanatoriums before returning to medical school, averaging over thirty months of hospitalization (Table 3).

The minor lesions, however, were not so innocuous as these figures suggest. One student with a minor lesion developed a small new lesion shortly after returning to school following twelve months of sanatorium care. Also, at least 2 students with minor lesions considered not to require hospitaliza-

TABLE 4 *Severity of Lesion according to Number of Cases Developing in Each Academic Year*

TYPE OF LESION	ACADEMIC YEAR OF DEVELOPMENT				
	ON ENTRANCE	FIRST	SECOND	THIRD	FOURTH*
Minor	4	0	2	4	3
Major	1	1	2	7	2

*The severity of many of the lesions developing in the fourth year could not be classified because of missing films.

tion subsequently developed, during internship, re-activations severe enough to require sanatorium care.

No clear-cut correlation could be found between the severity of the lesion and the academic year of discovery or between the severity and the original tuberculin reaction (Tables 4 and 5).

On the other hand, correlation between severity of the lesion and method of detection was striking. Of the 31 cases in Classes 1936 to 1948 the method of detection is known in 25. Thirteen were found on routine chest x-ray examination, and 12 only after the appearance of suggestive symptoms. Of the former, 1 was classified as major and 12 as minor, and in the 12 detected on the basis of symptoms the distribution was directly reversed, 11 being major and 1 minor (Table 6). All 11 major cases

TABLE 5 *Severity of Lesion according to Tuberculin Reaction on Entrance*

TYPE OF LESION	NO OF POSITIVE REACTORS	NO OF NONREACTORS
Minor	7	3
Major	6	5

discovered on the appearance of symptoms occurred prior to the institution of the semiannual routine examinations, 5 students were tuberculin reactors on entrance, 5 were nonreactors, and 1 was not tested because of a known previous lesion. Four of the 5 reactors had negative chest films on entry

and were therefore subject only to voluntary annual examination before their fourth year. All 4 developed symptoms in their third year. By means

TABLE 6 *Severity of Lesion according to Number of Cases Discovered by Two Methods*

TYPE OF LESION	DISCOVERED ON ROUTINE X-RAY EXAMINATION*	DISCOVERED BY SYMPTOMS
Minor	12	1
Major	1	11

*A routine x-ray film is one taken at stated periodic intervals or because of a recently acquired positive tuberculin reaction discovered in the routine survey.

of the annual tuberculin retesting of negative reactors, it was possible to determine the interval between a previous negative reaction and the onset of symptoms. Of the 5 nonreactors in the annual retest who developed tuberculosis, 3 developed symptoms within a year (five, eleven and eleven months), 2 developed symptoms four and eleven months after the annual tuberculin test had shown a positive reaction.

The contrast between the results of the program of voluntary annual x-ray examination and those of the present compulsory annual and more recent semiannual examination is striking since the in-

TABLE 7 *Severity of Lesions according to Number of Cases Detected by Annual and Semiannual Case-Finding Programs**

TYPE OF LESION	ANNUAL EXAMINATION	SEMIANNUAL EXAMINATION
Minor	8	5
Major	13	0

*The case finding program refers to that in operation at the time the lesion was detected. It does not consider the actual method of detection of the individual lesions, many of which were recognized by the appearance of symptoms despite the program in force at the time.

stitution of the present program there have been 5 cases of pulmonary tuberculosis, 4 of which were detected by routine chest film and tuberculin test and 1 following a hemoptysis, all 5 students had minor lesions.

A breakdown of the 26 cases of known severity according to the program in force at the time of detection is given in Table 7. The elimination of the previously preponderant major cases under the present regime is noteworthy.

Tuberculin Test

Tuberculin tests on entrance showed an average of 51.7 per cent of students to be reactors (Table 8). A steep downward trend, leveling off or perhaps even reversing in recent years, presumably represents a lowering of tuberculous infection in the college-age population, associated with a decrease

dents remains a major medical problem. The incidence of significant active adult-type pulmonary tuberculosis in Harvard Medical School was 2.2 per cent.

Although the nature of the tuberculin reaction of medical students on entrance played no demonstrable role in the subsequent development of pulmonary tuberculosis, the conversion from the non-reactive to the reactive state while in medical school carried a liability greater than 5 per cent that the disease would develop before graduation.

Slightly over 30 per cent of students who entered Harvard Medical School as nonreactors became tuberculin reactors before graduation.

Although the number of cases of pulmonary tuberculosis discovered in the last two years of the medical-school course was four times as great as the number developing in the first two years, the incidence of acquisition of tuberculous infection was about the same (12 or 13 per cent annually) for each academic year. This constant annual attack rate suggests that factors other than opportunity for infection are responsible for the fourfold increase in cases of pulmonary tuberculosis during the term of clinical training.

The duration of disability caused by the pulmonary lesion was closely correlated with the severity of the lesion at the time of its discovery.

Lesions detected by the appearance of symptoms were of greater severity and carried a far greater period of disability than those discovered by any routine method.

The rapidity of progression of the disease in medical students is such that many lesions become symptomatically evident, and are thereby detected, in intervals between routine examinations made only annually.

The adoption of a program in which surveys are made at intervals more frequent than once a year led to the elimination of almost all symptom-detected cases and of all major lesions. It is our belief that a semiannual examination represents the maximum interval for routine re-examination by x-ray examination or tuberculin tests not only for medical students but also for nurses and interns.

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lesions and virtually eliminated the cases detected on the basis of symptoms. Since the institution of the present program, there have been 5 cases of pulmonary tuberculosis, 4 of which were detected by the routine examination and 1 by the occurrence of hemoptysis. All 5 were minor lesions. If the asymptomatic cases had been allowed to continue until a later examination, or until the development of overt symptoms, it is not inconceivable that some students would have developed major lesions.

By means of the annual tuberculin test it was possible to determine the number of students who became infected each academic year. It was anticipated that more students would become tuberculin reactors during the clinical years, owing to greater exposure on the wards and in the autopsy room. Badger and Spink²¹ estimate that over 600 tuberculous patients are admitted annually to the general wards of one teaching hospital in Boston. At the same hospital 7 per cent of all autopsies performed up to 1941 showed active tuberculosis as a primary or contributing cause of

hours of physical and mental exertion. It must also be kept in mind that each academic year the medical student enters an age group whose mortality and estimated morbidity rate become increasingly high.²⁶ Unfortunately no adequate figures are available for the incidence of tuberculosis among carefully studied groups of the same age who are subject to the same conditions of living as well as to physical and mental exertion. As Rich²⁵ has emphasized in none of the published studies of graduate students in nonmedical fields are diagnostic criteria, thoroughness of study and duration of survey completely satisfactory. Only when adequate long-term surveys are made may one safely estimate the special risk of tuberculosis among medical students as contrasted with that among comparable groups of students not pursuing medical studies.

The lack of correlation between the nature of the original tuberculin reaction and the probability that active pulmonary tuberculosis will develop in medical school is of considerable interest. Experimentally it has been demonstrated that a previous infection

TABLE 10 *Annual Attack Rates according to Classes*

CLASS	SECOND YEAR TEST				THIRD-YEAR TEST				FOURTH YEAR TEST			
	NO OF NONRE- ACTORS	NO RETESTED	NO OF REACTORS	PER- CENTAGE OF REACTORS	NO OF NONRE- ACTORS	NO RETESTED	NO OF REACTORS	PER- CENTAGE OF REACTORS	NO OF NONRE- ACTORS	NO RETESTED	NO OF REACTORS	PER CENTAGE OF REACTORS
1940	62	62	7	11	55	52	7	13	45	45	11	24
1941	51	49	4	8	45	45	5	11	40	39	3	8
1942	71	71	6	8	65	61	11	18	50	50	5	10
1943	85	83	12	14	71	69	6	9	63	47	5	11
1944*	59	59	10	17	49	44	8	18	36	33	5	15
1945*	68	65	7	11	58	58	6	10	52	46	5	11
Totals		389	46			329	43			260	34	
Averages				12				13				13

*The third-year and fourth-year figures for these two classes are based on two tests made six months apart.

death.²² Heavy contamination of air near tables where fresh tuberculous tissue is examined has been repeatedly demonstrated.²³ In New York State 10 per cent of all deaths from tuberculosis occur in general hospitals,²⁴ and in Massachusetts, Dufault²² has estimated the figure at 20 per cent.

Despite greater opportunity for infection during the clinical years, an unexpected constancy in the attack rate (12 to 13 per cent) was found for each academic year. This uniformity indicates that there is equal opportunity for infection throughout each year. The predominance of cases of pulmonary tuberculosis in the third and fourth years has always been explained by greater exposure during those years. The constancy in annual attack rate seems to argue against greater exposure as the sole cause of the predominating number of cases during the clinical years; it is well known that factors other than opportunity for exposure operate in determining whether tuberculosis develops. A possible explanation is the accumulation of recently infected students whose primary lesions remain quiescent until clinical training is begun, when the lesions become reactivated because of the longer and irregular

offers some degree of protection against a subsequent infection under some conditions,^{25, 27} but offers undue susceptibility under others.^{28, 29} Furthermore, aside from such acquired resistance or hypersensitivity, it might be expected that fewer cases would appear among tuberculin reactors because this group has been challenged and has weathered the infection, whereas the nonreactor group has yet to demonstrate its native resistance. Such factors might be balanced by the possibility of endogenous recurrence in the reactor group. Reports in the literature on the incidence of tuberculosis in exposed groups of reactors and nonreactors vary from a greater incidence in the former^{30, 31} to a greater incidence in the latter,^{32, 33} or show no appreciable difference in the two groups. In the present study, the absence of appreciable difference between groups suggests that the nature of the original reaction presumably played only a minor role under the conditions studied.

SUMMARY AND CONCLUSIONS

The application of efficient case-detection methods shows that pulmonary tuberculosis in medical stu-

patient sought medical advice was nine months, and the total average delay for all cases before the diagnosis was established was seventeen months. There was a delay of from one to three months in 52 cases, including a few in which there was a delay of less than a month. There was an average delay of four to six months in 39 cases, of seven to twelve months in 48 cases, of thirteen to twenty-four months in 23 cases, of twenty-five to forty-eight months in 8 cases, of forty-nine to sixty months in 8 cases, and of sixty to one hundred and thirty-two months in 14 cases.

The relative culpability of patient and physician for the delay could not be established in all cases, but in 127 cases the patient was responsible for an average delay of nine months, and in 72 cases the blame for an average delay of seventeen months rested on the physician.

In 46 cases, or 24 per cent, the first x-ray examination failed to establish the diagnosis. A diagnosis of ulcer was rendered in 28 cases (14 per cent), with a resultant average delay of fourteen months before the final diagnosis was made, although 6 of these patients were operated on immediately. A diagnosis of ulcer with a question of cancer was made in 6 cases (3.1 per cent), with a resultant average delay of almost three months, although 3 of the 6 patients were operated on immediately. In 10 cases (5.2 per cent) a report of no disease was rendered, with a resultant delay of fifteen months. In 1 case a diagnosis of diverticulum of the stomach was made, and in another a diagnosis of gall-bladder disease. Both patients were subjected to immediate operation.

Study of the clinical histories in these cases revealed that epigastric pain or burning, epigastric distress or fullness and indigestion were the first symptoms in 131 (70 per cent) of the series. Anorexia occurred in 17 per cent, weakness or fatigue in 14 per cent, vomiting in 10 per cent, weight loss in 7 per cent, dysphagia in 6 per cent, and hemoemesis in 5 per cent.

In 17, or 8.8 per cent, a history of typical ulcer was given, and in 52 (27 per cent) a history suggestive of ulcer was obtained, making a total of 69, or 36 per cent, in which the ulcer syndrome was reproduced or suggested.

The implications of this analysis are clear. Apart from the failure of the patient to seek medical advice, a major source of error contributing to delay in establishing the diagnosis of cancer of the stomach is an astonishing degree of willingness on the part of physicians to treat, without x-ray examination or other investigation, patients in the cancer age group who have indigestion, epigastric pain or distress. From a study of the histories in these cases, it seems clear that patients whose symptoms were suggestive of ulcer were treated on that basis, and that those whose symptoms were so indefinite as to suggest insignificant functional disorders were

treated by various forms of dietotherapy and usually with alkaline powders. This casual method of dealing with such complaints has become widely known to the public and, in combination with advertisements for patent remedies, is undoubtedly a factor in the high incidence of self-treatment.

There is obviously a great lack of appreciation of the serious import of such symptoms in persons past the age of forty-five, and insufficient familiarity with the frequency with which such symptoms herald the presence of cancer, on a purely statistical basis.

Rivers,⁷ in a significant paper, has emphasized the fact that indigestion occurring in patients over forty-five years of age is frequently due to cancer. In an analysis of 2448 patients in various age groups who presented themselves with the symptom of indigestion, cancer of the stomach was found to be the cause in 8.8 per cent of patients from forty-five to forty-nine, in 10.8 per cent of those from fifty-five to fifty-nine, in 24 per cent of those from sixty to sixty-four, and in 36 per cent of those over seventy.

It is difficult to believe that anyone familiar with these figures would be willing to risk treatment of a patient with dyspepsia without benefit of searching investigation. It is essential that this information be disseminated, and it is necessary to reiterate that dyspepsia in patients over forty-five is a grave symptom.

Another source of error is an exaggerated notion regarding the accuracy of roentgenologic diagnosis. It is often stated that intragastric lesions can be accurately diagnosed in 90 to 95 per cent of cases. On inquiry, however, it seems clear that this high degree of accuracy is attainable only in large centers, where roentgenologists of exceptional experience and skill are available, and even then only when questionable cases are subjected to repeated examinations. This is not to decry the great value of roentgenographic diagnosis, but it is essential to point out that, in the hands of the average roentgenologist, such accuracy in diagnosis is not approached. In this series there were wrong diagnoses in 24 per cent, and Engel⁸ has stated that in this type of examination there is an admitted error of 20 to 25 per cent. In any patient in whom the diagnosis of gastric cancer is suggested, repeated x-ray examination at short intervals is imperative if the patient's symptoms persist.

The differential diagnosis of gastric ulcer and ulcerating gastric cancer merits special consideration. In fact the whole question of the management of gastric ulcer needs to be reviewed. A growing body of evidence suggests that there is an irreducible error in the neighborhood of 10 to 14 per cent in the roentgenologic diagnosis of this disease. Kirklin,⁹ emphasizing a point that is obviously not appreciated by the average clinician, writes as follows:

DYSPEPSIA, ULCER AND GASTRIC CANCER*

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IN 1928 Sir Berkeley Moynihan¹ wrote, "Not a little of the incredulity of patients and the apathy of medical men is based upon the undisputed conviction that cancer of the stomach is incurable." When it is realized that under the favorable circumstances existing in large metropolitan hospitals only 5 of every 100 patients who apply for treatment are cured of their disease, this becomes understandable, perhaps, but is still not justifiable. It is an undoubted fact that most practitioners of medicine have never seen a cured case of gastric cancer but that they have seen large numbers of patients die of the disease. When one recalls that this disease accounts for a third of all deaths from cancer, numbering approximately 40,000 cases yearly in this country, no further argument regarding its importance appears to be necessary.

The insidious character of gastric cancer is often put forward as the reason for this pessimistic picture, and although it is unquestionably true that in a small percentage of patients the disease is beyond the possibility of surgical extirpation when the first symptom manifests itself, study of the clinical histories reveals that in most cases symptoms have been present for months or years before the diagnosis is established. The culpability for this delay in establishing the diagnosis rests not only on the patient who fails to seek medical advice during the early stages of the disease but also in large measure on the physician who is satisfied to treat the patient medically for months or years without benefit of the searching investigation that is imperative in all such cases.

As Mullen² has pointed out

It is an unfortunate fact that most persons consider a mild degree of gastric discomfort to be a normal part of the process of growing older, and the words "indigestion" and "dyspepsia" to most minds signify an uncomfortable but entirely benign process. Yet within these two words lies the whole story of early gastric cancer symptomatology.

It is also true that this attitude is shared in large measure by many physicians.

The significant factor that is clearly responsible for the delay in the diagnosis of gastric cancer is the unfortunate circumstance that early cancer of the stomach shares with benign gastric lesions and functional disorders the symptoms of dyspepsia or indigestion as an early manifestation. This dyspepsia may be indefinite, or may simulate to a slight or marked degree or may mimic exactly the syndrome associated with benign peptic ulcer. The

resemblance of gastric cancer to the classic ulcer syndrome has been general knowledge for many years. In 1906 Graham³ wrote as follows: "In the later nineties our attention was strongly attracted by the many long histories of 'dyspeptic trouble' that preceded cancer of the stomach, and the thought that ulcer was this precancerous condition became firmly implanted." In 1909 Moynihan⁴ reported that 2 of every 3 patients with cancer of the stomach on whom he had operated had had a previous history of ulcer. Despite the fact that these observations were made forty to fifty years ago, their implications have not been widely appreciated or seen in proper perspective in relation to their obvious bearing on early diagnosis. The more recent literature continues to emphasize the frequency of ulcer or symptoms of ulcer in the clinical histories of patients with cancer of the stomach. Blackford⁵ reported that 38 per cent of his patients presented histories of preceding ulcer, and Eusterman⁶ stated that in 47 per cent of proved cases of gastric cancer encountered at the Mayo Clinic, the history was that of the accepted syndrome of benign ulcer. Whether the natural course of the disease in these cases is a degeneration of a previously benign ulcer or peptic ulceration of a slowly growing cancer or a prolonged precancerous state, distinct from ulcer, is a matter of secondary importance. The significant point is that in a substantial percentage of cases a long history exactly mimics or closely resembles the accepted syndrome of ulcer.

The present study is based on the records of 192 patients with carcinoma of the stomach seen in private practice and at the Massachusetts Memorial Hospitals. Since the majority of these patients were referred for consideration of surgical treatment, these cases represent a selected series, and this fact is reflected in a somewhat higher resectability rate than is usually reported. Seventy-seven cases were suitable for resection—a rate of 41 per cent. Twenty of these, however, were palliative resections, and 57 were resections for cure—in the latter group, the resectability rate was 30 per cent. Thirty-three cases were classed as inoperable, 60 were found to be inoperable on exploration, 18 were suitable for palliative procedures only, and 20 were suitable for palliative resections, 4 patients refused operation. Thus, in a relatively favorable, somewhat selected series of 188 patients in whom the ultimate status was determined, 111 (70 per cent) were hopeless when first seen by the surgeon.

Long delay before the diagnosis was established was almost the rule. The average delay before the

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Large numbers of patients with gastric cancer have lost their lives because their disease was confused with benign ulcer. A more aggressive approach to the problem of gastric ulcer should result in the salvage of many such patients.

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VAGINAL URETERAL ORIFICES*

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TRUE supernumerary kidney is a rare anomaly.¹ In a review of the literature Headings and Palmer² found a total of 44 cases, of which 6 had extravascular ureteral orifices. A case reported by Shane³ and the following case bring the total number of cases of supernumerary kidney with a vaginal orifice to 8.

A. G., a 7-year-old girl, was seen because of urinary incontinence, which had been present since birth but was apparent only when the child was on her feet. There had been no nocturnal enuresis since the age of 2. With the patient in the supine position there was no evidence of urinary leakage, but examination when she was standing revealed an intermittent spurring of urine from what appeared to be a ureteral orifice in the vestibule of the vagina. Intravenous urography (Fig. 1) showed a supernumerary kidney on the left, located above a normal-functioning left kidney. A ureteral catheter introduced into the vaginal orifice ascended to the pelvis of the upper left kidney. Ureteronephrectomy disclosed a true case of supernumerary kidney. Convalescence was uneventful and was not followed by urinary leakage since. It should be pointed out that this child had been examined by several physicians, but always in the supine position, and that the family had been continuously reassured that she would outgrow this disability.

In 1937 Eisendrath and Rolnick⁴ found in the literature 88 cases in which the ureter opened in the vaginal vestibule and 55 cases with opening into the vault of the vagina or the uterus. Since then, 6 cases⁵⁻⁷ have been reported, bringing the total to 61.

D. C., a 35-year-old housewife, was admitted to the hospital complaining of lifelong incontinence of urine. The amount, although not excessive, was sufficient to require the wearing of a vulva pad at all times. The patient had been married for 7 years but had no children, a finding that is not unusual in cases of vaginal urinary leakage.

Physical examination was negative, except for urinary leakage from the vault of the vagina (not from the urethra).



FIGURE 1 Case 1. The intravenous urogram shows a supernumerary left kidney with a vaginal ureteral orifice.

Laboratory study revealed normal findings. Intravenous urograms (Fig. 2) showed a normal right kidney, but no

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Such ulcers designated as benign, without qualifying adjectives are designated so — but with the implication that as no marks of malignancy are discerned, the lesions are probably benign, although malignancy cannot be positively excluded. The fact that 10 per cent or more of gastric ulcers are found microscopically to be malignant has been publicized thoroughly, and the roentgenologist feels that his diagnosis may not have been misleading, for he assumes that every ulcer will be considered as potentially malignant until proved innocent.

It is undoubtedly on the basis of this apparently irreducible error in roentgenologic interpretation that Allen and Welch¹⁰ found carcinoma in fourteen per cent of 277 cases diagnosed as ulcer. Judd and Priestley,¹¹ in a similar series of 237 cases in which a diagnosis of benign gastric ulcer was made, found cancer on exploration in 19 (8 per cent) and in 146 cases diagnosed as benign ulcers that were treated medically, 10 per cent of patients subsequently developed gastric cancer. The wisdom of treating medically any lesion that carries a 10 to 14 per cent chance of being malignant seems open to serious question. The approach of Judd and Priestley¹¹ in evaluating the relative risks attending medical versus surgical treatment for lesions diagnosed as gastric ulcer seems to go far toward clarifying this sharply debated subject. In a further analysis of 146 cases treated medically, they found that only 47 per cent of patients considered themselves cured, an additional 16 per cent had no symptoms if the medical regime was followed constantly, 5 per cent had gastric ulcer on x-ray examination, 11 per cent were operated on because of failure of medical treatment and had ulcer, and 10 per cent (14 patients) presented definite evidence of cancer. Of these, 7 died of metastatic cancer, the remainder were explored surgically, and in only 3 could the cancer be removed. In contrast, of 162 patients with gastric ulcer treated surgically who were followed for from one to five years, only 1 classified the result as unsatisfactory.

In the past few years there have been increasing reports of large series of gastric resection for benign ulcers of the stomach and duodenum, with mortality rates well under 5 per cent. Counsellor, Waugh and Claggett,¹² Judd and Priestley,¹¹ Jordan and Lahey,¹³ and St. John¹⁴ reported rates of 1.3, 2.5, 2.7 and 3 per cent respectively, and McKittrick, Moore and Warren¹⁵ reported a series of 94 cases without a death.

If one assumes that the results of surgical treatment are at least as good as those of medical treatment, with an operative mortality of 3 to 4 per cent, and balances against this the facts that with medical treatment 10 to 14 per cent of patients develop cancer and that a significant percentage have perforations and serious hemorrhages, — some of whom die, — it seems difficult to escape the conclusion that gastric ulcer, at least in patients over the age of forty-five or fifty, should be considered primarily a surgical problem. Of course each case is an individual problem, and exceptions should be made in patients who, because of advanced age,

obesity or coexisting disease, must be regarded as poor surgical risks. Certainly, a more radical attitude toward this disease will yield a significant increase in the percentage of cured gastric cancer, for Allen and Welch¹⁰ have shown that the cure rate for cancers encountered in operation on supposed ulcers is double the prevailing rate. The advantages resulting from the greater use of surgery in dealing with ulcerating gastric lesions, of course, depend on the maintenance of a low operative mortality. Rates such as those cited above can be expected only in the hands of experienced gastric surgeons.

In a certain percentage of ulcerating gastric lesions, the roentgenologist makes a diagnosis of gastric ulcer but suggests that cancer cannot be ruled out. In such cases the patient is frequently subjected to a therapeutic trial on medical treatment, the clinical response being observed, the stools watched for the presence or absence of occult blood, and after an interval of two or three weeks the change in the roentgenographic picture noted. This method of management is advocated by most gastroenterologists, including Jordan¹⁴ and Eusterman,¹⁷ who states that the results of medical treatment are only slightly less decisive than those of operation and histologic examination in establishing the diagnosis of ulcer or cancer. My experience with therapeutic trial, as well as that of many others, does not support this belief. Ulcerating cancers often respond so favorably — both clinically and in the rapid diminution of the size of the ulcer — as to lead one to the conviction that the lesion was benign. At best, when the result of therapeutic trial suggests that the lesion is malignant and operation is advised, a delay of from four to six weeks or longer is frequent.

The chief objection to the therapeutic method, however, is that the end results do not bear out the contention of those who advocate it. Eusterman¹⁷ reports the development of cancer in 10 per cent of medically treated ulcer cases not limited to patients in the cancer age or to patients in whom the suspicion of cancer is greater than average.

To one accustomed to dealing with cancer, a diagnostic method that depends for its success on observing the continued growth or persistence of a malignant tumor, in spite of treatment for weeks, has little to recommend it, such a procedure may have been amply justified when gastric resection carried an operative mortality of from 15 to 20 per cent, but with a mortality in the neighborhood of 3 per cent, the risk of medical treatment of a malignant tumor must be carefully weighed.

A hopeful fact is that much of the delay in the diagnosis of gastric cancer is susceptible of correction. It is obvious that the grave significance of dyspepsia occurring after forty-five must be stressed persistently in undergraduate and postgraduate medical teaching, and that the public must also be made aware of this hazard.

THE USE OF STREPTOMYCIN IN COLON-BACILLUS PERITONITIS*

Report of a Case

S RICHARD MUELLNER, M D,† AND ALEXANDER RUTENBERG, M D ‡

BOSTON

THE recorded clinical experience with streptomycin is as yet quite meager. The technic of administering this drug and the dosage to be employed in infections with various bacteria have not yet been established. The variation in susceptibility of different strains of the same bacteria and the rapid development of fastness in experiments in vitro suggest that a clinical evaluation of these factors is desirable.¹⁻³ The pooling of clinical experience

coli on smear and culture. The urine from the right kidney was sterile. An attempt was made to expedite the passage of the ureteral stone by dilatation of the ureter through cystoscopic means. Four days later however, the patient had sharp left-flank pain, chills and high fever, which proved to be due to the sudden passage of the stone from the calyx into the upper fifth of the ureter, the infection being thus bottled up in the left kidney. An immediate ureterolithotomy was done. At operation the retroperitoneal tissues were edematous, and the ureter was swollen. The ureter was incised over the stone and after the stone was extracted, thick green pus which contained *Esch coli* on culture, drained from the

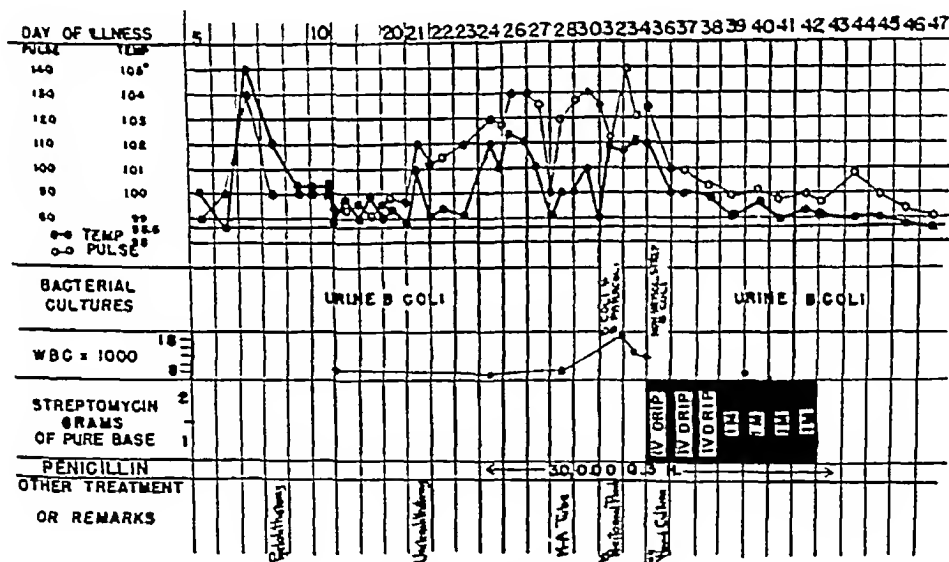


FIGURE 1 Clinical Course

Note the effect of streptomycin on the temperature, pulse and white-cell count

with streptomycin in carefully studied cases therefore seems to be worthwhile. It is with this purpose in mind that the following report is presented

CASE REPORT

W S (BIH 67286), a 50-year-old man, was admitted to the hospital because of pain in the left flank of 3 months' duration, associated at its onset in July, 1945, with chills and fever. Urologic investigation revealed a stone in the lower calyx of the left kidney and another stone at the left ureterovesical junction. The urine from the left kidney and from the bladder was full of pus and contained *Escherichia*

kidney. Following this operation the patient made an uneventful recovery.

It then became necessary to remove the stone at the ureterovesical junction, to prevent the establishment of a permanent ureteral fistula as a result of the previous ureterolithotomy. Consequently, 12 days later, the lower left ureter was exposed through a Gibson incision. In this region the retroperitoneal tissues were also edematous. The peritoneum itself, however, was extremely thin. Despite gentle retraction 2 small holes were inadvertently made in the peritoneum. These were at once closed by suture. The ureter was then incised, the stone was extracted, and the wound was closed around a drain.

The postoperative course was stormy. The patient developed unmistakable signs of peritonitis with paralytic ileus—a rather infrequent complication after this type of surgery. A peritoneal tap revealed cloudy fluid containing pus and *Esch coli* on smear and culture. Despite intubation of the small bowel by a Miller-Abbott tube, adequate chemotherapy with penicillin and sulfonamides, parenteral fluids

*From the Urologic Service, Beth Israel Hospital. The streptomycin used in this case was supplied through the courtesy of Dr. Gladys L. Hobby of the Charles Pfizer Company, Brooklyn, New York.

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function was apparent on the left side. The left lateral wall and dome of the bladder were deformed by extrinsic pressure. A pelvic left kidney was immediately suspected. Gynecologic examination revealed a moderate-sized fibroid uterus, but no mass could be identified as kidney. The ureteral opening in the vagina was found deep in the vault and on the anterior wall. With much difficulty a No. 5 Fr ureteral catheter could be passed about 15 cm. Skiodan was injected and ascended to about the level of the bladder deformity (Fig. 3). This seemed to confirm the tentative diagnosis of pelvic kidney, and a low-left-rectus incision was accordingly made, the left ureter being easily picked up. Dissection was carried down to the vagina and up as far as possible with this type of incision, no kidney was encountered. The peritoneal cavity was opened to permit better palpation of the abdomen. The right kidney was normal, but the left kidney fossa was empty. The bladder deformity was found to be due to the fibroid uterus. A diagnosis of aplastic left kidney was made, and about 8 cm. of the distal ureter was removed after double ligation with black silk. The proximal end was transplanted through the rectus fascia, so that if hydronephrosis developed, the ureter could be readily picked up and catheterized, and the location and character of the kidney determined prior to ne-

In the cases reported above, careful attention to the case history and scrupulous inspection were sufficient to lead to the correct diagnosis.



FIGURE 2 Case 2 The intravenous urogram shows a normal right kidney, no apparent function on the left and deformity of the left side of the bladder

phrectomy. This was never necessary. Six months after operation the patient was well, and for the first time since birth there was no urinary leakage.



FIGURE 3 Case 2 This film shows the left ureter following the injection of skiodan into the vaginal ureteral orifice

SUMMARY

One case of supernumerary kidney with a vaginal ureteral orifice is described, and one of an anomalous ureteral opening in the vaginal vault, making the total numbers of such cases reported 8 and 61, respectively.

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Epidemiological Board³³² Over 6000 ASTP students in widely scattered parts of the United States received one dose of 1.0 cc of a bivalent anti-A and anti-B vaccine prepared by concentration of the virus in infected chorioallantoic fluid, inactivated with formalin. An equal number of subjects served as controls. Influenza A in epidemic form appeared in each group at varying intervals, from twelve days before to five and a half weeks after vaccination was undertaken. Taken as a whole, the observed incidence of influenza among the inoculated was only 31 per cent of that in the controls (morbidity rates of 2.22 as against 7.11 per cent). The ratio of cases in inoculated subjects and controls varied greatly in individual groups, however, from a high of 1.60 (1.15 vs. 6.93 per cent morbidity) to a low of 1.15 (5.25 vs. 7.88 per cent). Best results were obtained when exposure to infection occurred a few weeks after vaccination, and at least a week's interval was necessary before any protection was evident. The poorest results were observed in the group experiencing the longest interval between vaccination and exposure to infection, but it is not entirely clear whether the relative failure in this group was due to the long interval or to other factors. Detailed reports of these studies present evidence that a multitude of factors determine the results to be expected following vaccination³³³⁻³³⁹. The conclusions to be drawn appear to be that immunization, with the vaccine employed, afforded a better than a three to one chance of protection, for a period of a few months, against the two most prevalent strains of influenza. A subsequent study, employing the same vaccine, indicated that protection may persist for as much as a year.³⁴⁰ Furthermore, in this study and another more recently reported,³⁴¹ the incidence of influenza among vaccinated subjects was from one fifth³⁴⁰ to one tenth³⁴¹ that in the controls. If these results can be confirmed, there will be a far more satisfactory basis for justifying the clinical use of the vaccine than has heretofore existed. Mass vaccination in the armed forces was wholly justifiable not only for the protection of large bodies of redeploying troops but also as a means of controlling what would have been an unparalleled opportunity for rapid and extensive spread of the disease if an epidemic had arisen. At present there is no apparent justification for widespread or routine use of the vaccine, in the absence of a clearly defined epidemic of influenza A or B. When a definite risk of exposure to either type of influenza exists, however, the vaccine may be used to protect persons whose circumstances warrant a special effort to prevent sudden illness, such as during the conduct of important personal or professional affairs and during travel. If the vaccine proves effective for as long as a year, its use on a large scale in the civilian population may deserve consideration — in the autumn of years that seem to be scheduled

for one of the periodic outbreaks characteristic of influenza in its present form. The recent experimental infection studies of Henle et al.³⁴² throw an interesting light on the possible results to be expected from periodic reimmunization with influenza, suggesting that primary and accelerated reactions, analogous to the different vaccination reactions associated with varying degrees of resistance to smallpox, may be observed.

The essentially localized nature of the lesions of influenza has led to some skepticism regarding the results that may be expected from any parenteral route of immunization. It is on this basis that various investigators have attempted to immunize by inhalation of modified virus.³⁴¹⁻³⁴³ Burnet et al.³⁴³ and Francis³⁴⁴ have shown that a factor in nasal secretions is capable of inactivating influenza virus, and it has been demonstrated that this mechanism is enhanced by parenteral immunization.³⁴⁵ It is fair to assume, therefore, that the production of an effective local resistance will be related to the production of a sufficiently high systemic level of immunity, but the surprisingly frequent finding of clinical influenza in persons exhibiting high antibody titers against the infecting virus has not yet been explained.

Local and constitutional reactions following administration of influenza vaccine have been widely observed, and are reported as occurring in from less than 1%³⁴⁴ to 59 per cent³⁴⁹ of different groups. These extreme differences apparently depend both on the definition of a reaction and on the pains taken to obtain reports. Constitutional reactions have been sufficiently frequent and severe, at all events, to indicate the need for modifications in either the product or the dosage schedule, or both. The possibility that divided doses increase the efficacy of the vaccine has been suggested by animal experiments,³⁴⁶ and would be expected on a theoretical basis. Antibody titrations on human subjects, however, have not borne this assumption out.³⁴⁷⁻³⁴⁷ In fact, Hare³⁴⁸ has suggested that secondary antibody responses from repeated doses of influenza vaccine are not to be expected, since the first injection is in all probability actually a booster dose for the great majority of subjects.

Several considerations warrant a conservative attitude toward the use of influenza vaccine, even if improvements in the vaccine should lead to a higher degree of protection over longer periods. Foremost among these is the possibility that sensitivity to the egg proteins in the vaccine will induce severe reactions. Among the 6000 ASTP students inoculated in the study referred to above, an asthmatic reaction occurred in only 1 case³⁴⁶ and an urticarial reaction in 1.³⁴⁸ At least one fatal reaction has been observed, however, following the use of a vaccine prepared from hen's eggs,³⁴⁹ and such reactions may be anticipated more frequently in persons receiving repeated booster injections of a vac-

and transfusions of blood, the clinical status became progressively worse. The patient remained distended, toxic and irrational. On the 15th postoperative day, when the patient's condition was most desperate, streptomycin was obtained, during the first 3 days 2,000,000 units were administered daily by constant intravenous drip, and the patient was given 500,000 units intramuscularly every 6 hours for 4 more days.

The effect of this therapy was most dramatic (Fig. 1). The temperature and pulse rate dropped at once, and the patient became rational. The abdominal distention receded, and the patient took nourishment and passed normal stools. The peritonitis seemed to have been completely eliminated by streptomycin. The urine, on the other hand, became sterile and free from pus for only 2 days after the initiation of the streptomycin therapy. Thereafter, despite the daily administration of 2,000,000 units of this drug for a total of 7 days, pus and *Esch. coli* continued to be present in the urinary sediment.

A few points in this case history are worthy of comment. The patient was rapidly failing because of a severe colon-bacillus peritonitis, which was uninfluenced by any of the sulfonamides. A fatal outcome was unquestionably prevented by the use of streptomycin. It is interesting that although the bacilli were apparently completely eliminated from the peritoneal cavity, permanent sterilization of the urinary tract was not achieved, despite the fact that the urinary tract was free from obstruction. The reason for this discrepancy is not clear. Experiments in vitro have demonstrated that bacteria

rapidly develop fastness to streptomycin.² The bacilli in the urine in the case reported above—but not those in the peritoneal cavity—apparently developed such a resistance. Whether the bactericidal effect of the streptomycin is affected by the character of the medium in which it acts (peritoneal exudate as against urine) or whether the peritoneum wards off infection more readily than the urinary tract remains problematical. The rapid development of bacterial resistance against streptomycin and the great variability in its bactericidal action against various strains of the same organisms¹ suggest that large initial doses are advisable for effective and permanent sterilization.

SUMMARY

A case of colon-bacillus peritonitis that was successfully treated with streptomycin is reported, and certain pertinent points are discussed.

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MEDICAL PROGRESS

ACTIVE IMMUNIZATION (Concluded)

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BOSTON

INFLUENZA

Following the identification of a virus agent causing human influenza,³¹⁴ efforts were made to develop vaccines effective in preventing or at least mitigating the infection. The finding of Burnet³¹⁵ that the fertile hen's egg provided a favorable medium for cultivating the influenza virus led ultimately to the use of this agent as the preferred culture medium. The demonstration that at least two distinct types of virus—designated "A" and "B"—could cause influenza^{316,317} posed the necessity of producing an effective bivalent vaccine. Numerous studies, usually with monovalent preparations, gave more or less equivocal results, whether the vaccine was administered subcutaneously³¹⁸⁻³²⁰ or by inhalation^{321,322}. There were occasional exceptions, as in the study by Henle et al.³²³ in which a striking degree

of protection was observed against influenza experimentally induced with a freshly isolated strain. A major improvement resulted from the discovery that the influenza virus could be efficiently concentrated by application³²⁴ of the chicken-cell-agglutination phenomenon observed by Hirst³²⁵ and McClelland and Hare,³²⁶ the preparation of virus suspensions of greatly increased immunizing potency being made possible. It had already been noted on occasion that vaccines of higher than average virus content appeared to give more promising results.³²⁰ Most of the succeeding studies, employing concentrated virus preparations,³²⁷⁻³³¹ produced higher immunity levels than had previously been attained, judged both by postvaccinal antibody titers and by resistance to natural or experimental infection.

Extensive confirmation of the value of a vaccine of this type was obtained in the study set up in 1943 under the Commission on Influenza, Army

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Use of impotent vaccine Smallpox vaccine is a living virus when properly prepared, and successful vaccination depends on the ability of this virus to multiply in the tissue of the vaccinated person. Multiplication of the virus in the host may fail for many reasons, including the following: improperly prepared vaccines (only by the practice of unceasing vigilance, even in a properly equipped and operated laboratory, is it possible to distribute a vaccine of consistently adequate potency, the operation of numerous small and inadequate vaccine establishments scattered through the Orient offers a possible explanation of the relatively frequent failure of vaccination seen in that part of the world³⁷⁰), improper storage of vaccine (vaccine virus, if refrigerated, lies dormant and retains its potency, but if allowed to warm up, it rapidly exhausts the metabolic resources of its suspending medium and dies, thus, failures to produce a successful reaction may be due to carrying the vaccine in the pocket or keeping it on a drugstore shelf—to be dependable, vaccine virus must have been stored at temperatures below freezing for as much of the time as possible, and the colder the temperature the better, since it is impossible to injure the virus by any available degree of cold), use of outdated vaccine (because it is usually not possible to keep smallpox vaccine continuously below 0°C at all times during shipping and handling, the vaccine necessarily undergoes some deterioration, and is therefore given a relatively short expiration date—for example, not over six weeks in Massachusetts—beyond which it cannot be regarded as dependable), and the use of less than the full contents of a capillary for each vaccination (this may result in failure, since on long standing the virus-laden lymph tends to separate from the clear glycerin portion, which is relatively inactive³⁷²).

Faulty vaccination technic A fully potent virus may fail to multiply in the vaccinated subject, because of any one of various errors in technic. Thus, the presence of such antiseptics as alcohol, mercurochrome and iodine on the vaccination site destroys the virus as soon as it is applied, and failure to achieve the right degree of penetration of the skin prevents the virus from obtaining a suitable site for multiplication. In a recent study in which two physicians used the same virus at the same time, one obtained twenty successful reactions out of twenty vaccinations, whereas the other obtained only six out of seventeen, the only difference being that the less successful physician failed to break the skin surface consistently with the needle.³⁷¹

Incorrect interpretation of the result obtained from vaccination A definite vesicle appearing at the site of vaccination is unmistakable evidence of a successful primary or accelerated reaction, but

the small papule characteristic of an immune reaction is less specific, and may be simulated by a traumatic reaction to the application of the needle. Furthermore, persons who have previously been vaccinated may exhibit a local allergic reaction to the antigenic substances in smallpox vaccine. A "dead" vaccine may thus induce a small papule, indistinguishable from an immune reaction except that it appears and disappears somewhat earlier.³⁷³ It is significant that the patients in the 23 cases of smallpox in the China-Burma-India Theater mentioned above were each recorded as having shown an immune reaction following vaccination, and similar experiences have been reported in the British Army in the Middle East.³⁷⁴ Indeed, Marsden³⁷⁵ says that the immune reaction should on no account be regarded as a successful result, since it does not necessarily indicate immunity, although often shown by immune subjects, and that persons who give this reaction but have histories that are at all uncertain should be vaccinated again and again. Marsden, however, acknowledges the validity of interpreting a deep-seated indurated swelling, developing about the third day and subsiding gradually, as a reaction of immunity.

Concerning the closely related subject of the person who cannot be vaccinated, d'Arcy et al.³⁷⁶ describe a hospital ship outbreak of 6 cases, in 5 of which the patients had recently been unsuccessfully vaccinated. Smith,³⁷⁷ the health officer meeting the ship at its first port of call, notes that in the prompt control of the outbreak, several persons were successfully vaccinated whose vaccinations had never previously been effective. One suspects that Dr. Smith was vigorous with the needle, indeed, it has repeatedly been recommended, particularly by British writers,³⁷⁸ that two or more insertions be employed whenever maximum protection against smallpox is urgent. Horgan and Haseeb³⁷⁹ have demonstrated, by the use of duplicate sites on previously vaccinated persons, that not all revaccinations produce the same result even under identical conditions at the same time, in their subjects the percentage of successful reactions, and hence the apparent ratio of accelerated to immune reactions, varied with the character of the virus preparation used. Nagler³⁸⁰ agrees with Horgan and Haseeb in recommending duplicate insertions on persons with a definite or probable history of previous vaccinations. It is worth noting at this point that a correlation between visible vaccination scars and resistance to smallpox in persons with histories of previous vaccination has been observed.³⁸¹ Some lay officials even require a visible vaccination scar as a basis for accepting a vaccination certificate.³⁸² This, of course, is unjustified, since vaccination by the multiple-pressure method usually leaves a scar that is subsequently difficult to find. The

cine of relatively short-lived effectiveness. It is to be hoped that from the experience of the armed forces a sufficient evaluation of allergic reactions to egg vaccines will have accumulated to determine at least tentatively the significance of such reactions. The possibility of employing eggs from ducks or turkeys, as suggested by Berkowitz³⁵⁰ for typhus vaccine, should be further explored.

Numerous modifications of the liquid concentrated allantoic fluid vaccine have been tried. Precipitation with alum³⁵¹ or protamine³⁵² did not appear to enhance the potency materially, whereas a vaccine suspended in oil^{347, 353} by Freund's method³⁵³ induced a rather high incidence of untoward local reactions. Salk³⁵⁴ has recently applied a technic long employed in potentiating antigens used in animal immunization, by adsorbing the vaccine virus on calcium phosphate, with preliminary results that appear promising. Such measures may prove particularly satisfactory when combined with improved methods of concentrating and purifying the virus. The differential centrifugation developed by Stanley³⁵⁵ appears to be highly effective, and further information on the alcohol-concentration method of Tovarnizky³⁵⁶ is awaited with interest. Improved means of inactivating the vaccine with minimal injury to its antigenic potency, such as the use of ultraviolet irradiation,^{346, 356} may further enhance the efficacy of the vaccine.

All the advances outlined above merely serve to increase the immunizing potency of the currently available egg-adapted strains of influenza virus. Burnet³⁵⁷ showed that egg adaptation is accompanied by fundamental changes in the biologic properties of the virus, and a far larger body of evidence than is now available will be required to determine whether such a modified antigen can retain its clinical effectiveness as well as the vaccinal modification of smallpox virus. Evidence already indicates that the influenza virus strains in current use for preparation of vaccines are antigenically somewhat apart from those isolated in recent epidemics.^{356, 358} Likewise, apparent antigenic differences between prevalent epidemic strains have been demonstrated.^{358, 359} The observations of Beveridge and Burnet,³⁶⁰ Shope³⁶¹ and others, however, suggest that, by selection of appropriate strains or by repeated vaccination, immunity of a broader antigenic pattern than that induced by single injections of the currently available vaccines is possible. It is well to bear in mind that the exact etiology of the influenza pandemic of 1918 is still unknown and, in all probability, will never be determined. No one can predict with assurance — although Shope³⁶¹ has made a brilliant approach to this problem — what the biogenesis of the next epidemic will be, and one is left to ponder the following still appropriate editorial comment³⁶² of three years ago:

Spectacular as have been the advances in recent years in research in influenza, it cannot be said that, faced with a disaster such as that of 1918, we are yet in a position to do anything very dramatic in order to prevent its spread. The virus responsible for the next pandemic will almost certainly be one that is unrelated to those now isolated. For this reason it will be necessary first to isolate the virus. This in itself may be a difficult proceeding, for a susceptible animal will first have to be found. Even supposing this proved to be possible, the manufacture of vaccine in sufficient time for use in the epidemic is — by all present indications — a sheer impossibility. And vaccines compounded from known strains will almost certainly be useless.

SMALLPOX

The continuing importance of maintaining adequate smallpox immunity, wherever one may be, is attested by reports such as that of the Hongkong epidemic of 1937-1938, in which 2000 persons died,³⁶³ of the Glasgow outbreak of 1942, which, although nipped in the bud, killed 24 per cent of those infected,³⁶⁴ of 5 deaths among 23 cases in American troops in the China-Burma-India Theater³⁶⁵ and of the recent outbreak of virulent smallpox in Seattle, imported by American troops returning from the Orient. One still occasionally hears the claim that the reduction in smallpox, where it has been achieved, is the result of improved sanitation. Rogers³⁶⁶ has outlined the fallacy of this argument so far as India is concerned, where decreases in smallpox morbidity are observed side by side with an unchanged prevalence of such diseases as cholera. Nor is it pertinent to claim that present-day smallpox is mild and therefore unimportant, for it is well established that the mild and severe forms may alternate in successive epidemics or coexist in the same one. Finally, the relation between the incidence of smallpox and the extent and effectiveness of vaccination laws has been so conclusively shown^{367, 368} that space will not be taken here to repeat the evidence.

The shifting populations of the recent war years have provided a fertile soil for transmission of smallpox and have put current vaccination programs and methods to a rigorous test. Although several incipient epidemics of smallpox resulting from these conditions were readily checked by vaccination, the small number of failures reported may serve as a basis for critical consideration of the requirements that must be met to achieve successful vaccination. In any such consideration it must again be emphasized that no immunization procedure is absolutely effective. The causes of vaccination failures can nevertheless for the most part be itemized, as follows:

Long interval since vaccination. The occurrence of smallpox in persons not vaccinated for many years merely points by contrast to the effectiveness of vaccination in persons also exposed who, having been vaccinated more recently, are found to be clearly protected.³⁶⁹

eruption," which in turn is indistinguishable from eczema vaccinatum, can arise from infection with the virus of herpes simplex⁴⁰⁵⁻⁴⁰⁷ Thus eczema vaccinatum should be regarded as a syndrome arising basically from eczema rather than from vaccination. Hershey and Smith⁴⁰⁸ point out the desirability of dropping the older clinical designations quoted above, specifying instead the virus and the underlying cutaneous disease, if any.

Although far rarer than generalized vaccinia, postvaccinal encephalitis is still observed occasionally in Europe and rarely in this country. Seven cases, 2 of which were fatal, were reported following some five hundred thousand vaccinations in the Edinburgh area in July, 1942.⁴⁰⁹ In Fife, on the other hand, 9 cases were observed in seventy-three thousand vaccinations.⁴¹⁰ Thus the incidence continues to vary tremendously in different series, in this country it can scarcely be greater than 1 in two hundred thousand. In dealing with such a rare condition, when the diagnosis is at best made by inference and when several known and no doubt several other unknown etiologic agents may induce a virtually indistinguishable picture, it is difficult to arrive at any significant conclusions. Although cases in infants do occur,^{411 412} the incidence is probably not over 1 in eight million.⁴¹¹ Moreover, encephalitis is extremely rare after revaccination.⁴¹¹ Hence it could probably be rendered even rarer by primary vaccination in infancy, which is also to be preferred for many other reasons. Treatment with convalescent serum has been used^{412 413} but is subject to the limitations mentioned under generalized vaccinia.

Postvaccinal tetanus has virtually been eliminated since the role of vaccination dressings, bunion pads, contaminated bone points and other factors in the etiology of this complication has been publicized. Nevertheless, the disregard of such well founded precautions is still occasionally followed by tetanus.⁴¹⁴ Miscellaneous complications continue to be related to vaccination from time to time,⁴¹⁵⁻⁴¹⁷ but without substantial evidence that the relation is more than coincidental.

RABIES

Any attempt to evaluate antirabic vaccination on the basis of available experimental or epidemiologic evidence is somewhat inconclusive, as shown in the extensive review by Webster⁴¹⁸ and compactly summarized recently by Casals.⁴¹⁹ The lack of extensive convincing evidence for the efficacy of rabies vaccine in preventing experimental animal infection was formidably exposed in Webster's thirteen-page table summarizing such experiments. Moreover, the epidemiologic data cited by Webster — derived chiefly from McKendrick⁴²⁰ — certainly do not provide any conclusive proof that antirabic vaccination protects human beings from the disease. Nor is there any comfort in the finding of

Denison and Dowling⁴²¹ in Alabama that rabies occurs with approximately equal frequency among Whites, who often seek antirabic treatment, and Negroes, who rarely apply for such treatment. Furthermore, these authors point out that among the 48 human deaths from rabies in the seventeen-year period considered, 23 occurred in persons judged to have received prompt and adequate treatment. They conclude that there is little relation between mortality from rabies and the administration of vaccine. On the other hand, the findings of Palik and Moss⁴²² that the mortality rate in treated persons was greater following bites from proved as against unproved rabid animals, from head bites as against bites elsewhere and in Negroes as against Whites, could be equally well explained by the assumption either that the vaccine gave only a partial protection or that it gave no protection whatsoever. Only their finding (confirmed by McKendrick's much larger series of cases) that delay beyond fourteen days in seeking treatment markedly increases the risk of death from rabies gives support to the belief that rabies vaccine is of value in human beings.

Such data, however, are by their very nature inconclusive. They may be influenced by a great variety of uncontrollable but highly important factors. First among these is the actual rarity of human rabies, 48 cases of any disease over a seventeen-year period,⁴²¹ for example, scarcely provide statistically significant data. Also, multitudinous factors influence the chances of infection: location of the bite, depth of the bite, entrance of saliva into the wound (as affected, for example, by clothing), local treatment applied, interval before seeking local or systemic treatment and so forth. Since such factors are always present in human exposure to rabies and since it will always be virtually impossible to obtain a properly controlled and statistically significant series of untreated cases, the evaluation of antirabic vaccination by epidemiologic methods must remain an unsatisfactory approach, and results based on this approach must be judged accordingly.

Regardless of statistical data, the experience of years has firmly established the belief, among all who have studied the problem, that antirabic vaccination greatly reduces the chances of contracting rabies. Webster,⁴¹⁸ after reviewing the lack of evidence for the efficacy of the vaccine, proceeds to furnish a detailed and elaborate schedule of the indications for vaccine treatment. And despite the fact that rabies is rare (no human case having occurred in Massachusetts, for example, since 1935), the disease is so horrifying to most minds and death from it is so absolutely certain that people continue to demand and physicians to administer the vaccine, with its attendant discomforts and risks, rather than face even a remote prospect of succumbing to rabies. It has little practical bearing on the case that most people think nothing of daily

responsibility must remain with the physician, to ensure that nothing less than a clear-cut immune reaction is observed before permitting a patient to risk exposure to smallpox.

Variations in the host-parasite relation. These can involve differences in vitality or specificity of the vaccinia virus employed, in the infectivity of the strain of smallpox encountered, and in individual response to the immunizing process. It is difficult to believe that 20 out of a group of 62 subjects exhibiting successful primary reactions could have manifested such reactions not more than fifteen months earlier, as reported by Minning,³⁸³ unless there were a qualitative difference in the two strains of vaccinia virus used. Stevenson,³⁷⁸ on the other hand, is inclined from analogy with animal studies to believe that the differences in protection observed following vaccination are due to differences in the immune response of the host. Evidence for such a concept is not readily adduced, but fairly convincing evidence has recently been presented that vaccinia virus strains of completely unrelated origin provide approximately equivalent protection against a virulent endemic strain of smallpox.³⁸⁴ For practical purposes, it is therefore wise to follow the simple dictum of d'Arcy³⁷⁸ that it is only the successful vaccination that counts, to persist in vaccinating until a successful vaccination is achieved, and to revaccinate at intervals of five to seven years and whenever vaccination is otherwise indicated.

Little can be said regarding the optimum age for vaccination, since few observations on this point have been made. Ratner⁴ offers the reasonable statement that the ideal time for vaccination is between three and six months of age and cites data regarding neonatal vaccination, mostly confirming the general impression that successful reactions at this age are undependable. It is almost universally agreed, chiefly for reasons given below, that vaccination should be performed not later than the first year of life.

At present virtually all smallpox vaccine available is prepared by inoculation on calves, carabao, sheep or similar herbivora, but the virus can be successfully cultivated in tissue media³⁸⁵ and the chorioallantoic membrane of the chick embryo.³⁸⁶ Vaccines have been prepared by both methods. Results with tissue-culture vaccine (inoculated intradermally) have been poor, the immunity being apparently quite transitory,^{387, 388} perhaps owing to an insufficient concentration of virus in the material employed. Chick-embryo vaccine has given promising results in the hands of several workers,^{379, 380, 389} is being employed on a limited scale in this country and elsewhere, and is strongly favored in principle by some investigators. One study with egg vaccine in this country indicated that the material employed induced a substandard immunity

and a deeper than average tissue reaction at the site of vaccination. Nagler³⁹⁰ on the contrary, observed that the reaction induced is more superficial than that produced by calf vaccine, and that immunity depends largely on the virus content, regardless of the source of the virus. One may safely predict that chick-embryo vaccine will be used on a much larger scale in the future, unless allergic reactions to vaccines derived from hen's eggs³⁴⁹ prove to be an obstacle.

Intracutaneous vaccination, as employed by Rivers and others^{387, 388} has been tried in the hope that immunity could be achieved without the necessity of producing a cutaneous vesicle. Results with chick-embryo virus given by this route have been little better than those with tissue-culture material.³⁹⁰ Even less promising were the results obtained with a formalinized vaccine.³⁹¹

Combinations of smallpox vaccine with other immunizing agents are rare, Blanchard³⁹² has reported the use of a mixed yellow-fever and smallpox vaccine. Combined immunization with smallpox and typhoid vaccines is a curiosity that has been reported by a Japanese,³⁹³ as one might almost expect—incidentally, the only modern report of peranal immunization for any purpose is also from Japan.³⁹⁴

Reactions, in a small percentage of persons vaccinated, continue to be reported from time to time. Autoinoculation on various body sites may occur in vaccinees,³⁹⁵⁻³⁹⁷ and is also occasionally observed among workers in contact with smallpox vaccine at this laboratory and elsewhere.^{398, 399} Thirty-four mild and miscellaneous skin eruptions were observed among two hundred and seventy-four thousand vaccinations in the Edinburgh outbreak.³⁹⁵ Several types of rashes occur, varying from a local erythema of greater or less extent that is a constant accompaniment of successful vaccination to lesions that embrace either the affected arm or other parts of the body⁴⁰⁰ and even to generalized vaccinia. Whether generalized vaccinia is to be distinguished from eczema vaccinatum is debatable, the excellent reviews of Jubb⁴⁰¹ and of McKhann and Ross⁴⁰² offer detailed discussions. The incidence of this complication is variously reported, but English and American figures⁴⁰¹⁻⁴⁰³ indicating that there is about 1 case in forty thousand vaccinations are representative. Since most cases appeared in eczematous patients and the mortality rate was disturbingly high prior to the advent of the chemotherapeutic drugs, it has been universally recommended that persons with eczema be protected from any contact with vaccinia virus, either direct or indirect, except when exposure to smallpox is likely. Treatment with convalescent serum has been employed⁴⁰⁴ but is of extremely doubtful value in this as in all other virus diseases. Furthermore, the syndrome is not always due to the vaccine virus. Recent case reports demonstrate that Kaposi's so-called "varicelliform

evidence on which this procedure is based and showed that, in experimentally infected guinea pigs, irrigation with a 20 per cent solution of soft soap is as effective as chemical cauterization with fuming nitric acid — and possibly even more effective. The administration of rabies vaccine is usually carried out in one of the following situations: a definite bite by a proved rabid animal, a definite bite by an animal in which rabies cannot be excluded — either the animal was lost track of or pathological examination was inconclusive, and any definite bite on the head or neck — treatment should be given while the animal is being observed and suspended if the animal is well seven days after the bite.

No general agreement exists regarding the possible channels of infection, besides definite skin-penetrating bites, that require treatment. Such situations may vary so widely that they are not subject to generalizations but must be considered individually.

Reactions to rabies vaccine have been reviewed by McKendrick⁴²⁰ and summarized by Webster⁴¹⁸ and Casals.⁴¹⁹ In slightly over a million treatments, major paralytic accidents occurred in 181 subjects (1 in 5861), and 48 were fatal (1 in 22,100). Neurologic complications were more frequent following the use of attenuated virus vaccines than with vaccines prepared from killed virus (1 in 3398 as against 1 in 8887). This supports the theory that such reactions are due to traces of viable and infective fixed virus. Kelser⁴⁴⁴ suggests that their occurrence with the use of phenolized (Semple) vaccine may be explained by the ability of phenol to coagulate proteins, so that occasional units of viable virus are left within a coagulated particle. Whatever the explanation, the occasional occurrence of these complications is sufficient contraindication to the administration of antirabic treatment unless there are clear-cut indications for its use.

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risking death (or, what is sometimes worse, survival) from spinal-cord injury or skull fracture following an automobile accident. Rabies remains a fear-inspiring menace in the mind of man, and will continue to do so whenever the possibility of contracting the disease exists.

Many of the inconclusive results reported following antirabic treatment were undoubtedly due to the use of ineffective vaccines. It is only within the last few years, beginning with Webster's development of a mouse test for measuring the immunizing potency of rabies vaccine,⁴²³ that evaluation of such vaccines and directed efforts toward their improvement have become practical. This method, which was found by others to provide a valid basis for distinguishing between potent and impotent batches of vaccine,⁴²⁴ was further developed by Habel⁴²⁵⁻⁴²⁷ and is included in the minimum requirements for rabies vaccine established recently by the National Institute of Health.⁴²⁸ Concurrently, various studies have been in progress on the improvement of rabies vaccines. Hodes et al.⁴²⁹ showed that an effective vaccine could be obtained from rabies-infected tissue inactivated by ultraviolet irradiation, and an improvement on this principle has been developed by Levinson et al.⁴⁷³ Meanwhile, Webster and Casals⁴³⁰ had made the not unexpected finding that the potency of a rabies-vaccine preparation depended to a large extent on its virus content. This finding has been confirmed,^{427 431 432} and probably explains the relatively high efficacy of Kelser's chloroform-killed dog vaccine,⁴³³ which contains a much larger amount (33 per cent) of brain and cord tissue than is ordinarily used. Furthermore, several investigators have found differences in the effective or immunizing properties of various strains of fixed virus^{426, 434} suggesting the importance of proper selection of strains for vaccine production. Hence, the prospects are that the quality of rabies vaccines available hereafter will be both superior to and more consistent than that of the vaccines of the last fifty years.

Further evidence of protection against rabies has been forthcoming in experimental and field use of the vaccine in dogs. A few years ago it was authoritatively stated that "as yet there is no authentic or convincing evidence that would lead to the belief that successful antirabic vaccination for dogs is available."⁴³⁵ However, Leach and Johnson,^{431 436} Damon⁴³² and others demonstrated that a good vaccine provides excellent protection against experimental infection, that a poor grade of vaccine provides only moderate protection and that unvaccinated control animals have a significantly greater fatality rate than the vaccinated groups. Furthermore, the field results are impressive. Beginning in 1937, over 6000 dogs a year have been vaccinated in Montgomery County, Alabama, simultaneously with a much less extensive program for disposal of stray dogs. The animal rabies incidences in this

county from 1936 to 1943, respectively, were 74, 23, 29, 0, 1, 0, 0 and 1. On the other hand, Mobile County, where dog vaccination was opposed, exhibited a continuously high incidence of animal rabies throughout this period.⁴³⁷ Experience in Massachusetts has been similar, although less extensive. Because the state laws make effective dog quarantine virtually impossible, a dog-vaccination campaign was begun in 1934 and stressed particularly in communities in or near areas reporting animal rabies. Either because of these inoculations or because of the natural rhythm in the rise and fall of the disease, cases of rabies in animals have declined since 1934, as indicated by the following figures:⁴³⁸

YEAR	NO OF CASES	YEAR	NO OF CASES
1930	310	1938	58
1931	304	1939	39
1932	131	1940	73
1933	171	1941	31
1934	331	1942	20
1935	278	1943	5
1936	136	1944	1
1937	211	1945	0

Dog vaccination, therefore, appears to furnish a promising means of controlling the principal reservoir of the disease. Occasionally, when rabies becomes seeded in wild animals,^{439 440} vigorous, specific eradication measures are highly effective in clearing up such foci. By and large, however, in a country such as the United States, where the disease cannot be kept out as in Australia and Hawaii, or eradicated as in England and Scandinavia, the best available measure for its suppression lies in building up the resistance of the dog population. Vaccination clearly does not provide a dog with absolute protection, but it does appear to increase the resistance sufficiently so that the minimal infective dose of virus is increased, and hence only the deeper bites, or those with an exceptionally high virus content, manage to infect. It has been pointed out by Anderson⁴⁴¹ for rabies, and by many others for diphtheria and other diseases, that if the frequency of transmission of a disease is reduced below a certain level, the disease tends to die out of itself. This is the rationale of continuing and extending the program of antirabies dog vaccination recommended by the Massachusetts Department of Public Health. Such a program must, for obvious reasons, go hand in hand with the elimination of stray dogs, some of the attendant problems of dog control and the ways in which they may be successfully surmounted have recently been pointed out by Hewitt.⁴⁴²

The decision whether to administer rabies vaccine depends on a number of factors, and there are many different recommendations regarding the exact rules to follow. It is universally recommended that the wound be cauterized with nitric acid. Shaughnessy and Zichis,⁴⁴³ however, questioned the

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32361

PRESENTATION OF CASE

A sixty-year-old housewife entered the hospital because of hematuria.

The patient was apparently well until three months before entry, when she fell, fracturing the left wrist. Following this accident she had a bout of painless hematuria, with the passage of small dark clots two or three times a day for three days. There was no concurrent frequency, urgency or other urinary symptoms. She remained asymptomatic until twenty-four hours before entry, when she suddenly passed bright-red blood while straining to urinate. During the night she urinated at hourly intervals, with some dysuria and difficulty in starting the stream. There was no incontinence, costovertebral-angle pain, chills or fever. She had had no previous urinary symptoms, and there was no recent weight loss, change in bowel habits or melena.

Twenty years before entry the patient had a tumor "filled with water" removed from the right lower quadrant of the abdomen. Seven years before entry, following a period of weakness, weight loss and slight postmenopausal bleeding, a hysterectomy was performed at a local hospital. She was not called back for a follow-up and received no x-ray treatment. She had had no vaginal bleeding since this operation. The menopause occurred fifteen to twenty years before entry.

On physical examination the heart and lungs were negative. There was slight tenderness in the suprapubic region. Pelvic examination revealed a second-degree perineal laceration and slight tenderness in the region of the bladder.

The temperature, pulse, and respirations were normal. The blood pressure was 160 systolic, 90 diastolic.

Examination of the blood showed a red-cell count of 5,050,000, with 90 per cent hemoglobin, and a white-cell count of 19,700, with 88 per cent neutrophils. The nonprotein nitrogen was 35 mg, and the total protein 6.5 gm per 100 cc. The chloride was 98 milliequiv per liter, and the carbon dioxide

26.9 milliequiv. The urine was grossly bloody and gave a +++ test for albumin.

Cystoscopy showed dark-red blood oozing from the right ureteral orifice. Clear urine was discharged from the left ureter. On the posterior wall of the bladder, in the midline and extending up to the dome and to the right, was a red, thickened area of mucosa covered by a layer of whitish slough or fibrin. A 3-mm papillary mass was seen in the center of this area. Several biopsy specimens from this lesion were reported as showing acute and chronic inflammation.

An intravenous pyelogram showed no excretion of dye on the right side over a period of sixty minutes. The left kidney was small and excreted the dye promptly. The bladder contained lobulated filling defects having the appearance of blood clots. There were multiple small calcifications in the spleen. A retrograde pyelogram showed obstruction of the right ureter 6 cm above the ureteral vesical junction, where there was a caplike defect in the upper margin of the dye (Fig 1). A plain film of the abdomen showed a large soft-tissue mass in the pelvis that reached to the level of the fourth lumbar vertebra and was consistent with a distended bladder; there were several dilated loops of small bowel. An x-ray film of the chest showed a considerable amount of fibrosis throughout both lung fields and two rounded areas of increased density in the left lung field.

The patient had several episodes of acute urinary retention and intestinal distention. An operation was performed on the eleventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. J. DELLINGER BARNEY: The fact that this patient had an episode of painless hematuria lasting for two or three days following a relatively minor fall may mean either that the fall was not so insignificant or that it lighted up some quiescent lesion in the kidneys or bladder. The absence of accompanying frequency, urgency or other symptoms tends to eliminate an inflammatory process. On the other hand the return of the hematuria some twenty-four hours after the initial episode, this being accompanied by considerable frequency, with dysuria and difficulty in starting the stream, suggests some inflammatory process arising subsequent to the injury. The absence of costovertebral-angle pain, chills and fever seems to rule out, or at least to decrease, the possibility of definite kidney infection.

Going on to the next item, the tumor "filled with water," which the patient said was removed twenty years before entry, may have been an ovarian cyst or something malignant, although the length of time that had elapsed since the operation rather tends to remove the latter possibility. The history of a hysterectomy seven years before entry for vaginal bleeding associated with symptoms of loss

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matory tissue cannot be avoided. I do not believe that the calcification seen in the spleen is of any particular significance.

The important observation, however, was that in trying to do a retrograde pyelogram definite obstruction in the right ureter at a level of 6 cm above the ureteral orifice was found. May I see the films?

DR. MILFORD D. SCHULZ: The films show non-visualization of the right kidney because of an obstruction in the lower portion of the right ureter, which is shown on attempted retrograde filling. The catheter apparently would not pass beyond the lowermost 6 cm of the ureter, where an irregular filling defect is lined by opaque material injected through the retrograde catheter. This has the appearance of a ragged non-opaque defect, possibly a polypoid soft-tissue mass, blood clot or stone. The soft-tissue mass seen arising from the pelvis on one film seems to be a distended bladder. Many defects in the visualized bladder are transient and are probably blood clots. The areas of density mentioned in the chest films may be metastases, but they are not too impressive.

DR. BARNEY: The record does not state whether any urine was obtained from the right kidney. The so-called "cap-like defect" in the dye that was injected into the right ureter may have been due to a variety of things. It may have been caused by a simple stricture, which was associated with more or less dilatation of the ureter. It may have been due to stone, which was either non-opaque or slightly so. It may have been caused by a neoplastic growth.

The films of the abdomen, which are said to show a large soft-tissue mass, may have indicated a neoplastic growth with adherent loops of small bowel or a full bladder. I am not able to interpret the various areas of density seen in the twenty-minute film of the bladder, especially the two or three that are just to the left of the midline. These may represent areas of calcification, either within the bladder or outside it. On the other hand they may be small collections of dye in the sacculi or folds of the lesion seen by cystoscopy. I do not believe, however, that these areas of density represent calcification. The films of the chest show fibrosis, and the two round areas of increased density in the left lung field may represent either tuberculosis or metastatic cancer.

I am not able to throw much light on the episodes of acute urinary retention and intestinal distention that occurred before operation. Again, however, all this may have been due to the fact that there was malignant disease outside the bladder in the pelvis, with adhesions between loops of small bowel and with a splinting, one might say, of the bladder so that it could not empty itself in the normal manner.

In looking over all these facts about the case I think one can say that the initial episode of hematuria originated in a lesion already existing in the bladder before the fall that the patient sustained. The onset of urinary symptoms, such as the dysuria and the difficulty in starting the stream, together with the nocturia, suggests a rather long-standing process in the bladder. I think that a kidney lesion can be ruled out, owing to the absence of the usual



FIGURE 2

kidney symptoms, such as pain and tenderness. The fact that there was no recent weight loss or change of bowel habits does not necessarily rule out cancer. I do not believe that the abdominal tumor removed twenty years before entry had anything to do with the present situation. I do, however, think that the hysterectomy, together with the history of weakness, loss of weight and vaginal bleeding, is suggestive of cancer of the uterus. The cystoscopic find-

of weight and weakness suggests malignant disease of the uterus, but the patient might have had fibroids

The white-cell count of the blood was considerably elevated, with a rather abnormal number of polymorphonuclears. The bloody urine was consistent with the history, and it is unfortunate that nothing

bladder strongly suggest a sloughing and infiltrating neoplasm, which was either primary or an extension from some other source. I say this in spite of the fact that several biopsy specimens showed only acute and chronic inflammation. It is possible that, together with the inflammatory tissue, there was neoplastic tissue. The statement that the intra-



FIGURE 1

more than blood and albumin was reported. One would like to know whether there were pus cells or bacteria. The fact that cystoscopy showed dark blood coming from the right ureteral orifice seems to limit the source of bleeding to the right kidney or ureter. Also, the clear urine coming from the left kidney, together with the x-ray appearances of a normal kidney on the left side, appears to eliminate the left kidney as a source of the hematuria. The conditions described on the posterior wall of the

venous pyelogram showed no dye on the right side in a period of sixty minutes indicates that the kidney was either entirely absent or was badly diseased. The lobular filling defect in the bladder, which was thought to suggest blood clots, is interesting but does not necessarily contribute anything more than the cystoscopic findings. The lesions seen in the bladder and shown by x-ray may, in fact, have been organized adherent blood clots, but the possibility of neoplasm or inflam-

lymphatic vessels or whether there was bacteremia, followed by pyelitis

During the patient's stay in the hospital the abscess increased in size, the temperature rose, and an operation was performed on the fifth hospital day. The sequence of infection, peritonitis, localization and abscess is quite clear cut. One is left with the problem of determining the cause of the infection that initiated this series of events.

The history gives several leads: the patient was known to have had ulcerative colitis, the onset of the illness coincided with the beginning of menstruation, and with the preceding period a less severe attack had occurred. Ulcerative colitis usually bears no relation to menstruation, at the time of menstruation, however, any chronic condition may be aggravated, and there is retention of water and swelling of the pelvic organs. Partial obstruction of the diseased bowel may therefore have followed, with perforation and the development of an abscess. Against this explanation is the fact that there was no real exacerbation of the colitis. Perforation due to ulcerative colitis occurs during an acute stage of the disease.

Perforation of the bowel due to a foreign body, such as a piece of wire or a pin, often occurs in the region of the ileocecal valve, but there is nothing in the history to suggest such a possibility. Carcinoma of the cecum may perforate and give a similar picture.

Because of the radiation of the pain upward and around the flank, kidney or ureteral difficulty should be considered. Carbuncles of the kidney do not point in this direction, and stones in the ureter rarely cause abscesses, so that any genitourinary process that developed must be considered secondary to an intraperitoneal infection.

The most frequent cause of right lower-quadrant discomfort — followed in a month by a severe attack and abscess formation — is acute appendicitis with perforation. The location of this abscess was typical of one of appendiceal origin, and the history was consistent with appendicitis. On a statistical basis this case can best be explained as acute appendicitis with perforation.

Acute cholecystitis, perforating peptic ulcers and acute pancreatitis cause right lower-quadrant abscesses, but there is little in the history to suggest any of these conditions.

The fact that the pain coincided with the onset of the last two menstrual periods is stressed. This may have no significance, but it may be a lead in discovering the cause of the abscess. Infection in or around the tube or ovary, which often flares up at the time of menstruation, could account for this clinical picture. The abscesses of pelvic inflammation often

localize in the right lower quadrant. Against this possibility is the statement that the patient was entirely well between the attacks of pain. The radiation of the pain is also against pelvic inflammation. Endometriosis, with secondary infection, is a rare condition that might have accounted for the abscess in this case.

My diagnosis is a right lower-quadrant abscess that was most probably secondary to an acute appendicitis.

DR LELAND S MCKITTRICK: When I saw this patient in consultation at the hospital, I could not be at all certain of the diagnosis. I thought that I could feel a mass in the lower abdomen, but I was not certain because of the slight distention and the well marked tenderness. There seemed every reason to suppose that the ulcerative colitis was not responsible for this particular episode. If there was an abscess it was believed that there was everything to gain and nothing to lose by avoiding immediate operation. The patient was much better on the following day, the distention subsided, gas was freely passed by rectum, and as the abdomen softened the mass was easily palpated. At the time of operation the diagnosis was ovarian cyst with a twisted pedicle. Pelvic abscess secondary to a ruptured appendix was the second choice.

CLINICAL DIAGNOSIS

Ovarian cyst, with twisted pedicle

DR INGERSOLL'S DIAGNOSIS

Ruptured appendix with pelvic abscess

ANATOMICAL DIAGNOSIS

Dermoid cyst of ovary, with torsion and infarction

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: Dr McKittrick's operative note was as follows:

A small, right muscle-splitting incision was made, the intention being to open into any abscess that was present or to permit a diagnosis if an abscess was not encountered. When the peritoneal cavity was opened a dark mass was presented having the physical characteristics of an infarcted tumor. The incision was then enlarged, and the adherent small bowel was carefully freed. The entire mass, which proved to be an ovarian cyst with one complete rotation of the pedicle, was then freed from the abdominal wall and surrounding structures. It was removed without difficulty. No further exploration was carried out.

The specimen we received was an obviously infarcted ovarian cyst measuring 12 by 8 by 5 cm. The wall was quite thick, and the lumen was filled with the characteristic sebaceous material and hair

ings indicate a lesion rather low down in the right ureter, and in the absence of stone or any evidence of a simple stricture, I think that this patient had a carcinoma of the ureter on the right side, probably metastatic from carcinoma of the uterus, with extension into the bladder. This may have accounted for the soft-tissue mass in the pelvis that was reported by the radiologist, but I confess that this finding does not impress me too much.

CLINICAL DIAGNOSIS

Carcinoma of ureter

DR. BARNEY'S DIAGNOSIS

Carcinoma of ureter, right, with extension into bladder (? metastatic from uterus)

ANATOMICAL DIAGNOSIS

Papillary carcinoma of ureter, right.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN The operation consisted of a right ureteronephrectomy. The ureteral obstruction, which had produced a moderate hydronephrosis, proved to be a grayish-yellow friable obviously carcinomatous mass 4 cm in length involving the entire circumference of the ureter and apparently completely occluding its lumen (Fig. 2). The wall was invaded, but the serosa was perfectly smooth. Microscopically it was a papillary carcinoma of the transitional type of epithelium that normally lines the ureter and bladder. There was no extrinsic tumor, and no involvement of the bladder. The defects seen in the bladder were almost certainly blood clots, because when the patient was last seen two months post-operatively, the bladder looked perfectly normal.

Papillary tumors of the renal pelvis and ureter have been known to implant in the bladder, although there still is some question whether the bladder lesions are implants or autonymous growths. Personally I am inclined to favor the latter thesis.

quadrant, with nausea and vomiting that lasted three days. The ache disappeared when the period ceased, and the patient was well until six days before admission, when the next period started. Five days before admission she noticed in the right lower quadrant a slight ache that within twenty-four hours developed into a severe pain, radiating around the right flank and up toward the right costal margin. She was nauseated, vomited frequently and was unable to retain anything by mouth for three days. The day before admission she felt better and retained some fluid. On the day of admission the pain was less severe and there was no vomiting. No stools or flatus had been passed for four days.

The abnormal findings on physical examination were confined to the abdomen and pelvis. The abdomen was distended, and there were moderate spasm and acute tenderness in the right lower quadrant. Rebound tenderness was referred to the right. There was a questionable mass in the right lower quadrant. Peristalsis was normal. Pelvic examination revealed acute tenderness in the right vault.

The temperature was 101.5°F, the pulse 108, and the respirations 22. The blood pressure was 110 systolic, 70 diastolic.

Examination of the blood showed 13 gm of hemoglobin and a white-cell count of 23,400, with 90 per cent neutrophils. The urine gave a ++ test for albumin, and the sediment contained 40 white cells, with frequent clumps, and 6 red cells per high-power field. The nonprotein nitrogen was 15 mg per 100 cc, and the prothrombin time 27 seconds (normal, 22 seconds).

The patient's condition remained unchanged. Dysuria developed on the second day, and there was gross blood in the urine. The temperature fell to 99°F, where it remained until the fourth hospital day, when it rose to 101.5°F. The white-cell count ranged between 19,000 and 25,000. The mass in the right lower quadrant became more definite and slightly larger.

An operation was performed on the fifth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS INGERSOLL The outstanding fact in this case is that a septic process developed. The onset was acute and severe, and the symptoms of peritonitis rapidly developed. Fortunately, this process was localized, and when the patient was admitted on the sixth day of her illness an abscess was present in the right lower quadrant and pelvis. The elevation of the white-cell count to 23,400, with 90 per cent neutrophils, indicates an excellent response to this infection. An abscess located over the course of the ureter may lead to urinary infection with dysuria and pyuria, which were present in this case. There is no indication of whether the infection invaded the urinary tract by extension through the

CASE 32362

PRESENTATION OF CASE

A forty-three-year-old housewife entered the hospital complaining of pain in the right lower quadrant of the abdomen.

The patient had had ulcerative colitis for about twelve years, with many remissions and exacerbations. The last episode of active colitis took place seven months before admission, when she was hospitalized for three weeks for study and treatment. After discharge she remained well until a month before admission. Coincident with the onset of the menstrual period there was an ache in the right lower

materials and more suitable ones will undoubtedly become available as time goes on and will probably be of the greatest help in working out many of the difficult but fundamental biologic problems that can best be solved through the use of such tracer materials. One can also look forward to considerable advances in the therapeutic use of radioactive materials.

"HIS ACTS BEING SEVEN AGES"

DR. MARJORY W. WARREN,¹ in a recent issue of the *Lancet*, has presented the case of the chronic aged sick, in whom, so often, "dull, apathetic, helpless and hopeless, life lingers on sometimes for years, while those round them whisper arguments in favour of euthanasia." This is not the picture that should be presented, nor will it be when we fully awaken to our responsibilities, which are new in their present magnitude. The aged infirm we have always had with us, but owing largely to the triumphs of medicine, the span of life has steadily lengthened, and because of the war and the entrance of women into industry, there is a shortage of young persons available to care for the aging population.

The better care of the chronic sick, and particularly the aged sick, is a medical responsibility that will in no wise decrease with time, for the expectation of life is constantly improving. Thus, in Great Britain the population of persons aged sixty or over has increased from less than 2,500,000 in 1901 to over 6,250,000 in 1944, and in the United States it is estimated that the 9,000,000 population of those sixty-five years of age or over in 1940 will increase to 22,000,000 in 1980. Since we have succeeded in prolonging human life, we must bend our energies to making that prolongation endurable. There is little doubt that the infirmities of age have been neglected and that too little effort has been made to diagnose and treat the illnesses of old people and to plan for what degree of rehabilitation may be found possible and practicable.

The aged, in their hospitalization, need wards that are designed to meet their physical circumstances, that simulate their accustomed surroundings and that are near their homes. They need diets suited to their age, and equipment adapted to their infirmities.

They need floors that are not highly polished, hand-rails about their wards and elevators or suitably graded stairways. The geriatric hospital ward should be used as a clearinghouse to the patient's or to an otherwise suitably conducted home, with a close and continuing follow-up. Never should the patient, regardless of age, who can be salvaged for whatever time is remaining be allowed to become bedridden.

Geriatrics should be as useful a specialty for the latter end of life as pediatrics is for the beginning years. In the words of the editorial² accompanying Dr. Warren's paper, "Given domestic help, nursing care and medical attention when needed, many old people who now die after years in hospital could live interesting and possibly useful lives at home, finally dying triumphantly in their own beds."

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MASSACHUSETTS MEDICAL SOCIETY BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

HARPIN — Raymond A. Harpin, M.D., of Lynn, died August 10. He was in his forty-third year.

Dr. Harpin received his degree from Boston University School of Medicine in 1931. He was a fellow of the American College of Surgeons.

His widow survives.

HOWLAND — George L. Howland, M.D., of Jamaica Plain, died August 7. He was in his seventy-seventh year.

Dr. Howland received his degree from Tufts College Medical School in 1897. He was a fellow of the American Medical Association.

LEE — Harry J. Lee, M.D., of Boston, died August 7. He was in his sixty-sixth year.

Dr. Lee received his degree from Boston University School of Medicine in 1904. He was a member of the staffs of the Newton, Cambridge and Hahnemann hospitals and the New England Hospital for Women and Children. He was a fellow of the American College of Surgeons and the American Medical Association.

His widow and two sons survive.

REID — I. Eugene Reid, M.D., of Jamaica Plain, died August 12. He was in his seventy-third year.

Dr. Reid received his degree from the University of Edinburgh Faculty of Medicine in 1897. He was a fellow of the American Medical Association.

His widow, a son and a daughter survive.

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ATOM BOMB AND MEDICAL RESEARCH

AS IN the case of other projects undertaken primarily for the conduct of war, many significant and far-reaching peacetime developments can be expected to result from the knowledge and materials acquired in the course of producing the atom bomb. Numerous developments of interest to biologists and to medical investigators will undoubtedly result from the fact that certain radioactive isotopes are now available in sufficient quantities for use in fundamental researches. Valuable contributions to physiology and therapeutics have already evolved as a result of the use of such isotopes produced in relatively small quantities with the cyclotron. The use of radioactive iodine in the treatment of thyrotoxicosis by Hertz and others and the studies of Ross and Gibson and their associates with radio-

active iron are examples of local contributions made possible with the materials and methods developed by Evans, Roberts and others at the Massachusetts Institute of Technology.

Those in charge of the Manhattan Project* have recently made a detailed announcement concerning the isotopes that will be available and the mechanism by which investigators may obtain them. It was pointed out that the production of tracer and radiotherapeutic isotopes is one of the great peacetime contributions of the uranium chain-reaction pile. Since the inception of the pile, these men have been cognizant of its peacetime potentialities, and since the end of the war, they have been active in attempting to realize these opportunities. Since, however, the war-built piles and wartime researches had other objectives, a considerable transition in developments and operations connected with the piles must be effected before the supply of radioactive isotopes can begin to meet the demand.

The limitation of the pile in making available pure radioactive substances must be emphasized. Most of the products being made available are not salvaged by-products of the plutonium process but are items requiring special production from processed irradiated uranium. In particular, the majority of the radio isotopes in greatest demand in biology and medicine, such as those of carbon, sulfur and phosphorus, must be produced by irradiation of materials that are foreign to the existing piles, which were not designed for this purpose.

Special committees have been set up and policies have been temporarily established for the distribution of materials as they become available. The chief criterion to be used in their distribution is the maximum benefit to the national welfare considering the limited amounts of radioactive isotopes that are on hand. They are to be distributed to individuals only through qualified institutions and organizations, which will be responsible for their proper use. Charges for the additional costs incurred in filling these requests will be made to the institutions in which they are used.

A list of the supplies of the various materials on hand and their properties was published. Additional

*Availability of radioactive isotopes. Announcement from Headquarters, Manhattan Project, Washington, D. C. *Science* 103:697-705, 1946.

resistant to sulfonamide therapy.⁵ The Department of Public Health has therefore voted to discontinue distribution of antimeningococcus serum. In conjunction with this change in policy, it is desirable to recapitulate the principal considerations in the treatment of suspected or proved cases of meningitis.

Diagnosis Treatment of meningitis varies according to the causative organism, specimens of cerebrospinal fluid and blood for bacteriologic examination must therefore be obtained before therapy is begun. The importance of early and accurate bacteriologic diagnosis has recently been summarized in the *Journal*.⁶

Drug therapy In any case of meningitis in which purulent fluid is obtained by lumbar puncture, it is advisable to administer penicillin. This drug should always be given to such patients intrathecally as well as intramuscularly.

Sulfonamides (sulfadiazine, sulfamerazine and sulfathiazole) are of definite value in the treatment of meningitis caused by the pneumococcus, streptococcus or *Haemophilus influenzae* (Pfeiffer bacillus) and are the agents of choice in the treatment of meningococcal infections. Early and adequate sulfonamide therapy (by mouth, or parenterally as the sodium salt, but not intrathecally) is therefore indicated in any case of meningitis pending bacteriologic diagnosis.

Precautions Because patients with meningitis are usually dehydrated as a result of vomiting, fever, sweating and failure to take fluids, it is essential to precede the first administration of any sulfonamide drug by the administration of fluids, given preferably by the intravenous or the subcutaneous routes and in sufficient amounts to overcome the dehydration. *Regardless of the sulfonamide drug selected or the route of administration, ample fluid output should be ensured by whatever means is most effective.* It is also advisable to administer sodium bicarbonate or lactate to prevent the precipitation of sulfonamides in the kidneys.⁷ Observance of these principles will help to avert complications, which otherwise frequently arise.⁸

Specific therapy When a bacteriologic diagnosis is established, specific therapy is recommended as follows, the agents being given in the order of preference.

Meningococcus Sulfadiazine, penicillin

Streptococcus Penicillin and sulfadiazine

Pneumococcus Penicillin, sulfadiazine and typhoid-specific antipneumococcus serum.*

H. influenzae (Pfeiffer bacillus), Type B Streptomycin, sulfadiazine and anti-*H. influenzae*, Type B, serum*, all three in combination

*Furnished by the Department of Public Health

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CORRESPONDENCE

AN UNUSUAL FOREIGN BODY

To the Editor: Dr. Miller's report of a rose stalk in a boy's neck, in the August 1 issue of the *Journal* recalls a somewhat similar case that occurred during my internship at Worcester City Hospital more than forty years ago.

A middle-aged Polish laborer was admitted to the Accident Room with a punctured wound of the right buttock. The patient's command of English, as well as that of the friends who accompanied him, being extremely limited, no history could be elicited except that "a stick had hit him." He complained of some pain but was otherwise in good condition. The wound was explored by the finger, but since no foreign body could be felt, it was believed to be a simple puncture. He was, however, kept for observation. On the third day he developed hematuria, on the fifth day signs of general peritonitis appeared, from which he died in a few days.

Autopsy showed a piece of wood over an inch in diameter that had entered through the right sacrospinous notch, transfixing the bladder and reached the obturator foramen on the left. Both ends were firmly fixed, and the pathologist was obliged to saw it to dislodge it from its position. It was blunt at both ends.

Later investigation showed that the patient had been working on some sort of wood-working machine when a large splinter flew off and entered his body, an extraordinary instance of centrifugal force.

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BOOK REVIEWS

The Biological Basis of Individuality. By Leo Loeb, M.D. 8°, cloth, 711 pp. Springfield, Illinois: Charles C. Thomas, 1945. \$10.50.

In this excellent book the author takes the position that it was necessary for one person to undertake this work, rather than to edit a collective book written by specialists in the different sciences that contribute the essential data; he appears to have succeeded admirably well in his effort. The subject is considered a mosaic of many tissues and organs, each functioning and metabolizing in its own peculiar way. The particular characteristic distinguishing one subject from another is designated as individuality differential. The author finds transplantation experiments best suited to analyzing differences as expressed in terms of individuality.

Individuality differentials on the one hand and organ and tissue differentials on the other are supported by references to comparative anatomy, embryology, genetics and biochemistry. The problems are discussed under the headings of transplantation of tissues in higher organisms, which furnishes the most delicate tests of individuality differentials, phylogenetic and ontogenetic development of individuality and organismal differentials, from the primitive to the highest organisms and from the egg to the adult state, conditions suggesting or simulating the presence of individuality differentials that exist in certain unicellular organisms, organismal differentials of tumors, which represent modified

MEDICOLEGAL ABSTRACT

Relation of Patient and Physician Liability for malpractice. The plaintiff entered the hospital in September, 1942, for rest and treatment for a nervous condition and other ailments brought about principally by acute gall-bladder attacks.

He was advised to consult the defendant, who gave him an electric shock treatment. On September 21, the defendant administered a second shock treatment. When the plaintiff recovered consciousness, he was suffering from severe pain in the right hip and thigh. This was called to the defendant's attention, but he ignored it until September 24, when x-ray examination showed a fracture of the right hip.

The plaintiff sued for negligence in the administration of the shock treatment and for negligence in the diagnosis.

At the trial the plaintiff presented no evidence other than that from which the above stated facts could be found. The defendant offered only the testimony of a doctor whom he sought to qualify as an expert on shock treatment. This witness had been an orthopedic surgeon for thirty years and had treated two hip fractures and one shoulder fracture resulting from shock treatment. He had also seen one spinal fracture resulting from shock treatment. He stated that he was familiar with the literature and reports of the medical profession on shock treatment and had talked with various specialists giving such treatment, but he admitted that he had never seen such treatment given and knew nothing of it of his own knowledge. He testified that fractures can occur in shock treatments despite every precaution taken to prevent them. The plaintiff excepted to the admission of this evidence on the grounds that the witness was not qualified as an expert on the subject of shock treatment.

The trial court ruled that there was no evidence from which a jury would be warranted in finding that the defendant had been negligent and directed a verdict for the defendant. The plaintiff excepted to this ruling, and carried both questions to the Supreme Court of Tennessee.

The plaintiff took the position that since all the equipment and instrumentalities used to administer the treatment were within the exclusive control of the defendant, it was fair to infer that his injury was the result of negligence, thus attempting to invoke the doctrine of *res ipsa loquitur*. The Court, however, decided that this doctrine is applicable only when the injury is not ordinarily explainable except by negligence—for example, when a plaintiff's eye was injured while he was unconscious during an appendectomy, or when a piece of the plaintiff's tongue was cut off in an operation for adenoids. Under such circumstances a layman could infer negligence without any explanation from an expert, but the court was of the opinion that a layman could

not determine, without the help of an expert, whether or not, without negligence, a fracture could result from shock treatment. The court also gave weight to the fact that in this case the uncontradicted evidence of the expert was that such an injury could occur without negligence. (A somewhat different view of the doctrine of *res ipsa loquitur* and of the effect to be given to the fact that a patient was unconscious at the time he was injured prevailed in another case*).

The Supreme Court decided that the witness had sufficient knowledge of medicine and medical literature to entitle him to rely on a textbook acquaintance with the subject matter of his testimony. He was qualified as an expert because he had sufficient knowledge of the subject matter, and the source of his knowledge therefore affected only the weight to be attributed to his testimony and not his qualifications to testify. (*Quinley v Cocke*, 192 SW [2d] 992, March 2, 1946, Supreme Court of Tennessee.)

*Medicolegal abstract. *New Eng J Med* 234:134, 1946.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

DISTRIBUTION OF ANTIMENINGOCOCCUS SERUM DISCONTINUED

Since the therapeutic value of sulfanilamide against meningococcal infection was first reported nine years ago,¹ it has been shown in many thousand cases that sulfonamides are the therapeutic agent of choice. As pointed out a few years ago in the *Journal*,² the mortality rates in groups of sulfonamide-treated cases frequently ran below 5 and rarely rose above 10 per cent—a result far superior to any that was ever obtained with serum therapy. Because of the remarkable efficacy of sulfonamide therapy in meningococcal meningitis, the Council on Pharmacy and Chemistry voted, in 1944, to omit antimeningococcus serum and meningococcus antitoxin from *New and Nonofficial Remedies*.³ Later in the year the following editorial comment⁴ was made:

Antimeningococcus serums are still used by some medical officers and civilian physicians, perhaps because they prefer to cling to tradition or because they assume that serum therapy is an essential part of "doing everything possible." There seems to be little if any reason for believing that this supplementary form of therapy is of additional benefit. Indeed there is increasing evidence that antimeningococcus serum, particularly when given by the intrathecal route, may actually do more harm than good in most drug-treated cases.

The demand for antimeningococcus serum in Massachusetts has practically ceased in the last two years, particularly since it has been shown that penicillin is a useful supplementary remedy in patients who are unable to tolerate sulfonamides or in whom the infective strain of meningococcus is

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ACUTE MYOCARDIAL INFARCTION

A Study of 100 Consecutive Cases

WILLIAM N. CHAMBERS, M.D.*

HANOVER, NEW HAMPSHIRE

THIS study consists of detailed clinical observations on 100 consecutive cases of acute myocardial infarction at St. Luke's Hospital, New York City. Eighty-five of these patients were observed from one to ten years prior to the initial attack, for an average of four years, either on the wards or as outpatients. Follow-up studies of from one to four years were made on 64 of the 66 survivors.

The criteria used for making the diagnosis were those enumerated by Shillito et al.¹ fever, tachycardia, leukocytosis, elevated sedimentation rate and electrocardiographic and blood-pressure changes.

So far as could be determined, the observers were dealing with the initial attack in each case. With the present study in view each patient was carefully observed, and detailed clinical and laboratory evaluations were made. Serial electrocardiograms were taken until the infarct was considered healed. Follow-up study consisted of a brief history, physical examination, blood pressure readings and electrocardiograms.

Thirty-four per cent of the patients died of the initial attack. The average length of life after admission was seven days, the longest thirty days, and the shortest seven hours.

There is considerable variation in the literature regarding the percentage of initially fatal cases, ranging from 20 to 47 per cent.²⁻⁴ By the end of the first year 42 per cent of the patients in this series had died, 8 per cent from recurrent attacks.

INCIDENCE

Occupation

No correlation was found between the type of occupation or environment and the incidence of acute myocardial infarction. Rathe⁴ found that

persons living in rural areas were affected as often as those in urban areas.

Age

The average age of patients in the complete series was fifty-nine years. The oldest in the series was ninety and the youngest thirty-five years. The average age was sixty and a half years for patients who died during the initial attack, fifty-nine for those who died of a recurrence within a year of the initial attack and fifty-seven and a half for those who survived one year or more without recurrence. Patients in the initially fatal group were on the average three years older than those who survived more than a year, and one and a half years older than those who succumbed to a recurrence within a year of the initial attack.

The effect of age on immediate mortality has been pointed out by many observers, including Woods,² Levine,³ Rathe,⁴ Cooksey⁵ and Baer et al.⁶ In Bland and White's⁷ ten-year follow-up the average age was sixty-one years for patients who died of the initial attack, fifty-seven (at the time of the initial attack) for those who died within ten years and fifty-one for those who survived ten years.

Sex

In this series there were 72 men and 28 women—a ratio of approximately 3 to 1, the usually accepted figure, although Willius⁸ found a ratio of 7 to 1. Twenty men and 14 women died of the initial attack, the relatively higher mortality for the latter (50 per cent) than for the former (27 per cent) may be explained by the fact that the initial attack usually occurs later in women than in men. The average age at onset of the initial attack was sixty-three years for women and fifty-seven and three quarters for men, a difference of over five years. In cases in which the initial attack was fatal the average was sixty-five and a half years for women and fifty-eight

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tissues, organismal differentials in the maintenance of harmony of the organism as a whole, and in the interaction of the organs and tissues within the organism, immune processes in their bearing on the interpretation of organismal differentials, relation between the evolution of species and organismal differentials, and significance of individuality differentials in the psychosocial field—in which the concept of individuality had its origin.

There is a useful bibliography, followed by an author and subject index. This book, when read with considerable thought, will yield great profit.

The Embryology of Behavior. The beginnings of the human mind. By Arnold Gesell, M.D., Ph.D., Sc.D. In collaboration with Catherine S. Amatruda, M.D. 8°, cloth, 289 pp., with 78 illustrations, 44 plates and frontispiece. New York: Harper and Brothers, 1945. \$5.00.

This book should prove to be of immense practical value to all students of human behavior. The authors develop their theme in true scientific spirit. They state "[We attempt] to indicate how an organic complexus of behavior is built up concomitantly with the bodily development of embryo, fetus and neonate. Adopting a thoroughgoing monistic approach, we are under no necessity of defining a casual interaction between body and mind. We simply assume that as the soma takes shape, the psyche likewise takes shape. We are dealing with a single developmental morphology."

The first chapter is devoted to an instructive brief historical survey of primitive, descriptive and experimental embryology. The subsequent chapters, which are written in a clear style and are fortified by sketches and drawings, concern birth and age, zygote and embryo, genesis of behavior, the archaic motor system, the growth of fetal behavior, breathing behavior, muscle tonus, electrotonic integration, the fetal infant, the circumnate infant, the diurnal cycle of sleep and wakefulness, species and individual, the dynamic morphology of behavior and the hierarchical continuum. A striking feature of the book is a photographic delineation of behavior patterns and growth sequences. The appendix gives an example of the investigation in outline with specimen protocols.

There is a working list of selective references for each chapter, as well as a useful index. When one considers the recent effect of experimental embryology on the understanding of the constitution and the emphasis on psychosomatic medicine, one realizes that this volume is a basic contribution in this direction. It should be on the shelves of every library.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Bone-Grafting in the Treatment of Fractures. By J. R. Armstrong, M.D., M.Ch., F.R.C.S., A/W/Comm. R.A.F.M.S., and surgeon-in-charge of an R.A.F. orthopedic and fracture center, registrar to the Orthopaedic Department and to the Fracture Clinic, Charing Cross Hospital, London, and registrar to the Metropolitan Hospital, London. With a foreword by R. Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S., civilian consultant in orthopedic surgery of the Royal Air Force. 8°, cloth, 175 pp., with 204 illustrations. Baltimore: Williams and Wilkins Company, 1945. \$7.00.

In this monograph the author has attempted to bring together in one volume material relating to the special subject of bone grafting in the treatment of fractures. The text is well illustrated, and there is an adequate index.

An Index of Differential Diagnosis of Main Symptoms. By various writers. Edited by Herbert French, C.V.O., C.B.E., M.A., M.D. (Oxon.), F.R.C.P., consulting physician, Guy's Hospital, assisted by Arthur H. Douthwaite, M.D., F.R.C.P., physician, Guy's Hospital. Sixth edition. 4°, cloth, 1128 pp., with 789 illustrations. Baltimore: Williams and Wilkins Company, 1945. \$17.00.

This standard reference work, first published in 1912, has been fully revised, and many new laboratory tests and diagnostic methods have been included in this sixth edition. A comprehensive, inclusive index of 214 pages is appended to the text, making it possible to find in this condensed volume any subject mentioned therein. The work should be in the libraries of all general practitioners as a reference source. It is printed with a good type on filled paper, which makes it rather heavy to handle.

NOTICES

ANNOUNCEMENTS

Dr. J. Penteado Bill announces the removal of his office to the Professional Building, 270 Commonwealth Avenue, Boston.

Dr. Frank S. Broggi, having returned from military service, announces the opening of his office in Portland, Maine, for the practice of neurology and psychiatry.

Dr. Thomas G. Connelly announces the removal of offices from 676 Adams Street, Dorchester, and 270 Commonwealth Avenue, Boston, to 375 Commonwealth Avenue, Boston, for the practice of internal medicine.

Dr. Albert Y. Kevorkian announces the reopening of his office for the practice of gynecology, female urology and obstetrics at 422 Beacon Street, Boston.

Dr. Charles Gale Shedd has returned from military service and is resuming the practice of surgery at 422 Beacon Street, Boston.

Dr. L. Robert Weiss announces the removal of his office from 483 Beacon Street to 68 Bay State Road, Boston.

SUFFOLK CENSORS' MEETING

The Censors of the Suffolk District Medical Society will meet for the examination of candidates at the Boston Medical Library, 8 Fenway, on Thursday, December 5, 1946, at 4:00 p.m.

ASSOCIATION OF MILITARY SURGEONS

The convention of the Association of Military Surgeons of the United States will be held October 9 to 11, inclusive, in Detroit. Among the highlights of the meeting will be addresses by Colonel Ervin Abel, president of the association, by the Surgeons General of the United States Army, Navy and Public Health Service and by Major General Paul R. Hawley, of the Veterans Administration.

Any past or present medical, dental or veterinary officer of the United States Army, Navy, Public Health Service or Veterans Administration is eligible for membership in the association on application to the secretary, Colonel James M. Phalen, United States Army (retired), Army Medical Museum, Washington 25, D.C.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 12

FRIDAY, SEPTEMBER 13

*10:00 a.m.-12:00 p.m. Medical Staff Rounds. Peter Bent Brigham Hospital.

12:00 p.m.-1:00 p.m. Clinicopathological Conference (Boston Hospital). Joseph H. Pratt. Diagnostic Hospital.

TUESDAY, SEPTEMBER 17

*12:15-1:15 p.m. Clinicoradiological Conference. Peter Bent Brigham Hospital.

(Voices continued on page xiv)

15 severe congestive failure. Thirteen patients were in shock. Friction rubs were heard in 6 cases. Three patients had ascites.

In the initially fatal series, rales and poor heart sounds were almost constant findings. Cyanosis occurred in over 66 per cent. More than 50 per cent of all patients in this series had some disturbance of rhythm, as well as extrasystoles and gallop. Of the 6 cases with auricular fibrillation, 4 were fatal. Edema was found in 50 per cent, and an enlarged liver in 33 per cent of fatal cases. Severe congestive failure, which appeared in 33 per cent of fatal cases, was infrequent in patients who survived and in those in shock. Four of the 6 cases with friction rubs were fatal. All patients with ascites died of the first attack of infarction.

X-ray study revealed cardiac enlargement in 76 per cent of the series. Master et al.^{9, 10} point out the importance of this factor in prognosis, a high percentage of patients with cardiac decompensation having enlarged hearts, the principal cause of death in coronary occlusion. They state that the favorable prognosis in young persons may well depend on the low incidence of cardiac enlargement. White and Bland¹¹ showed that there is a direct correlation between cardiac enlargement and mortality.

Although extrasystoles and gallop rhythm in themselves had no great effect on prognosis their persistence increased the gravity of the prognosis.¹²

There seemed to be a slight difference in the findings on admission between patients who died within a year and those who lived one year or more, disturbances in rhythm and signs of cardiac decompensation appearing more frequently in the former.

Pulse and Temperature

On admission the average pulse in the fatal cases was 115, rapid pulse usually persisted until death. The average rectal temperature for this group was 101.7°F, and the temperature remained elevated until death. In only 1 fatal case was there no evidence of tachycardia, and fever was present in all fatal cases.

The pulse in the surviving patients averaged 100 and remained rapid for an average of eight days, the temperature, which was slightly over 100°F on admission, usually fell to normal on the ninth or tenth day — one or two days after the pulse returned to normal.

Blood Pressure

Hypertension occurred in 74 per cent of the entire series, a rate definitely greater than that expected for the general population in this age group. The incidence was roughly the same in fatal (71 per cent) and nonfatal (77 per cent) cases. Hypertension at the onset of the attack was a frequent finding, being present in 53 per cent of the series, and was noted oftener in the fatal (68 per cent) than

in the nonfatal cases. Hypotension at the onset of the attack was a comparatively infrequent finding, occurring in 18 per cent of the cases.

A fall in blood pressure usually occurred following the attack, but the blood pressure often remained within hypertensive limits. The fall was usually immediate, but was sometimes delayed as long as seven days after the onset of the attack. An early return of blood pressure to normal or hypertensive levels was a good prognostic sign. The blood pressure usually did not return to its former levels in the fatal group. The number of survivors in whom the original hypertension recurred increased with time, 58 per cent had regained their hypertension by the second year. After recovery from the initial coronary occlusion the level of the blood pressure had no effect on the frequency of recurrence or on the ultimate prognosis.

LABORATORY FINDINGS

White-Cell Counts

The average white-cell count in the fatal cases was 20,000, reaching a peak by the second day. It invariably remained elevated until death. In the patients who survived, it averaged 13,000, the peak being reached on the first day, and the elevation being maintained for about ten days. The white-cell count was above 15,000 in 40 cases. Of the patients with counts between 15,000 and 20,000, 12 died and 12 survived. Of those with counts of 20,000 to 25,000, 5 died and 4 survived. Death occurred in all patients with counts over 25,000. The highest white-cell count was 39,000.

Sedimentation Rates

The erythrocyte sedimentation rate, which was elevated in 90 per cent of the nonfatal and in all the fatal cases, was in general no higher in the latter than in the former. Of the 38 patients whose rates exceeded 50 mm per hour, 24 survived and 14 died. There were 5 cases with rates over 100 mm per hour, only 1 of which was fatal. The highest rate of 128 mm occurred in a patient who survived.

Electrocardiograms

Tracings were taken on admission and subsequently on alternate days until stabilization, which usually occurred between the second and the third week. After discharge tracings were usually taken at intervals of three to six months.

Acute changes were found in all cases, 52 showing the anterior-apex type (Q₁ T₁), 40 the posterior-base type (Q₂ T₂) and 8 a combination of both types. The mortality was higher in the anterior-apex type (24 cases, or 47 per cent) than in the posterior-base type (15 cases, or 38 per cent). In patients with a combination of both types, the mortality was 100 per cent. Vander Veer and Brown¹³ found a nearly equal occurrence of anterior and posterior infarction patterns, but a significant percentage of the fatal

for men. For women the immediate mortality was greater and increased with advancing years.

HISTORY

A past history of symptoms referable to the cardiovascular system was found in 84 per cent of cases, the average duration of the symptoms being four years. Dyspnea was the most frequent symptom, being present in 44 per cent of cases. Anginal pain was present in 40 per cent, and symptoms of cardiac decompensation of varying degrees in 12 per cent. Most of these cases had been observed at this hospital prior to the initial attack in decompensation. Other prominent symptoms were easy fatigability and palpitation, which are usually reported.⁴ Hypertension was known to have existed in 74 per cent of cases.

Diseases appearing before the myocardial infarction were diabetes (13 per cent), syphilis (6 per cent), cerebral hemorrhage (5 per cent), and cancer (4 per cent). There were 3 cases of polycythemia vera, 2 of myxedema, 2 of glomerulonephritis, 2 of duodenal ulcer and 1 each of pernicious anemia and sprue. The presence of these diseases was demonstrated either in this hospital or by records from other hospitals. Three cases of cholecystitis were proved at operation, but 9 patients gave complaints suggestive of this condition. No patient on whom autopsy was performed showed evidence of acute or chronic cholecystitis. Some type of major surgical operation had been performed prior to the attack in 5 per cent of cases, but in no case did the onset of acute myocardial infarction appear to bear any relation to such procedures.

SYMPTOMS

Chief Complaint

The most prominent chief complaint was pain, which occurred in some form in 79 per cent of cases, 56 per cent of patients gave substernal pain as the chief complaint, 12 per cent complained of substernal pain and dyspnea, and 8 per cent had epigastric pain. There were 2 cases of right-upper-quadrant pain. Dyspnea was the second most prominent chief complaint, occurring in 26 cases — alone in 7, with weakness in 4, and with orthopnea in 3. Other chief complaints were syncope (3 cases), overwhelming fatigue and weakness (2 cases) and nausea and vomiting (1 case). It is of interest that pain was not even mentioned as a chief complaint in 21 per cent of cases. Substernal pain was the chief complaint in 80 per cent of patients who survived and in only 50 per cent of fatal cases. Of the 8 cases with epigastric pain, 5 were fatal. Severe dyspnea and orthopnea occurred more frequently in the fatal than in the nonfatal cases.

Nature of Pain

Investigation of the nature of pain revealed the following types of substernal pain: constricting,

of mild to moderate severity, 52 per cent, severe, crushing, 11 per cent, boring, 3 per cent, and choking, 3 per cent. Constricting pain occurred with equal frequency in the fatal and nonfatal cases. No correlation could be made between the intensity of pain and prognosis — of the 11 cases with complaint of severe to excruciating precordial pain, none was fatal. On the other hand, 21 per cent of the entire series of patients had no pain, of whom approximately 50 per cent died of the initial attack.

Epigastric pain was described in 8 cases, localization of pain in the epigastrium is apparently associated with a grave prognosis, for 5 of the 8 cases with this complaint were fatal.

Radiation of Pain

In this series radiation of pain occurred three times more frequently than nonradiation. The most frequent type was down the left arm. Other types were down the right arm, down both arms, up to the neck and into the jaw. When the pain occurred in the epigastrium or right upper quadrant, it did not radiate.

An attempt to correlate the radiation and death showed that radiation occurred in 83 per cent of nonfatal and 57 per cent of fatal cases, in the former, radiation was three times more frequent than nonradiation. Radiation to unusual areas occurred oftener in the nonfatal than in the fatal cases.

Duration of Pain

The time that elapsed between onset of pain and hospitalization varied considerably: seven and a half days for patients who had no pain, five and two thirds days for those who had intermittent, and eighteen hours for those with constant pain. Patients with pain were hospitalized earlier than those without pain, and, in general, patients who survived were hospitalized earlier than those who died.

Other Symptoms

Although pain was the outstanding chief complaint, other symptoms were prominent. Eighty-six per cent of patients had dyspnea of varying degrees, 50 per cent had weakness, and over 33 per cent had sweating. Nocturnal dyspnea, orthopnea, ankle edema, nausea and vomiting, which were present either singly or together in approximately 25 per cent of cases, appeared to have more effect than pain on the immediate prognosis, over 50 per cent of patients with these symptoms dying of the initial attack of infarction.

PHYSICAL FINDINGS

Physical examination on admission disclosed poor heart sounds and congestive rales in approximately 75 per cent and cyanosis in slightly less than 50 per cent of cases. Edema of varying degrees and disturbances of heart rhythm were noted in 33.3 per cent. Eighteen patients had enlarged livers, and

rences within this period were older (fifty-nine years) than those who had no recurrences (fifty-seven years). Men appeared more susceptible to fatal recurrence than women. The number of recurrences varied between one and three, the majority having only one in the period of observation.

The symptoms of cardiac decompensation were outstanding in the cases of fatal recurrence. Eighty-seven per cent were either on digitalis or had some symptoms of cardiac decompensation. Angina was present in only 50 per cent of this group.

In the cases of nonfatal recurrence angina was the outstanding symptom, being present in 88 per cent. Forty-four per cent of these patients either were on digitalis or had some symptom of cardiac insufficiency. Only 16 per cent of patients without recurrence either were on digitalis or had some symptom of cardiac insufficiency. Angina was present in approximately 50 per cent of these cases. Other complaints were infrequent, 22 per cent of these patients having no symptoms.

It is striking to note that the symptoms of cardiac insufficiency were most frequent among the fatally recurrent cases (75 per cent), much less frequent in patients who had nonfatal recurrences (33 per cent) and almost negligible in those who had no recurrence (8 per cent). Some degree of dyspnea was a fairly constant complaint in all three categories. Angina was more frequent in the cases of nonfatal recurrence than in either those of fatal recurrence or those of nonrecurrence.

In more than 50 per cent of Rathe's⁴ late fatal cases the patient had congestive heart failure, of the survivors only 20 per cent had this condition. In Bland and White's⁷ ten-year follow-up study, of the 30 per cent who survived 33.3 per cent had complete recovery, 33.3 per cent had angina, and 33.3 per cent had dyspnea.

No correlation could be made between the severity of the symptoms in the initial attack and the number of recurrent attacks, except for the cases of cardiac decompensation. The severity of the symptoms did not increase with the recurrences, whereas the incidence of decompensation did increase, and the prognosis was worse for those who had this condition. Decompensation, which was often not present during the first attack, usually appeared during the second.

Over 50 per cent of the patients who survived a year, with or without recurrence, were working, either full or part time. This percentage is lower than that given by Cooksey,⁵ who found that more than 75 per cent of the survivors returned to a useful occupation. Master et al.,¹⁷ in a series of 202 cases, reported that 50 per cent of the survivors were able to return to work.

AUTOPSY FINDINGS

The results of autopsy were reported in 18 cases, 15 in the initially fatal and 3 in the recurrent group.

In all cases there was evidence of acute myocardial infarction, with the exception of 1 case in which a healed infarction was found. Sixteen cases showed definite evidence of coronary occlusion. In only 1 case was there evidence of occlusion of both arteries. The left coronary artery was involved in 62 and the right in 38 per cent.

In Baer and Frankel's¹⁵ series 70 per cent showed anterior, 23 per cent posterior, and 7 per cent antero-posterior occlusion.

Mural thrombus, ruptured posterior wall of right ventricle, aneurysm of left ventricle and interventricular septum, pericarditis and pulmonary embolism were found in 1 case each. In no case did autopsy show the gall bladder to be involved, although 3 patients had complained of gall-bladder symptoms during life.

SUMMARY AND CONCLUSIONS

Clinical observations in 100 cases of acute myocardial infarction are presented.

The older the patient at the time of the initial attack, the more serious the prognosis. The incidence was higher among men than among women, but mortality was higher among women, whose attacks tended to occur later in life.

In patients who gave a past history of cardiac decompensation the mortality was higher. The long-standing presence of angina or dyspnea had no particular influence on the prognosis.

Although pain was an outstanding chief complaint, it was not present in 21 per cent of the cases. In the fatal cases only 25 per cent of patients had severe precordial pain. Excruciating precordial pain, if not intractable, did not carry a poor prognosis, intractable precordial pain and epigastric pain occurred often in the fatal cases. Radiation of pain had no relation to mortality.

The symptoms of excessive dyspnea, orthopnea, nausea, vomiting, excessive fatigue or weakness were found in over half the initially fatal cases. Such symptoms appeared to be more significant than pain in the immediate prognosis.

The physical findings of edema, enlarged liver, ascites and disturbances of rhythm carried a poor prognosis. Fever and tachycardia were always present in the initially fatal cases.

The incidence of hypertension was greater in patients with coronary occlusions (74 per cent) than in the general population. There was no correlation, however, between antecedent hypertension and mortality rate.

The sedimentation rate, which was of help in establishing the diagnosis, was elevated in 90 per cent of cases. The height of the sedimentation rate, however, bore no relation to the prognosis. The white-cell count, which was of help in both diagnosis and prognosis, was elevated in 90 per cent of the initially fatal and in 70 per cent of the non-fatal cases. With counts between 20,000 and 25,000

cases were of the anterior variety Levine and Rosenbaum¹⁴ noted that anterior infarction was more frequent in the initial attack than later In Baer and Frankel's cases¹⁵ 52 per cent were of the anterior and 34 per cent of the posterior type Rathe⁴ observed a definite predominance of anterior and indeterminate electrocardiographic patterns in early fatal cases Willius⁸ and Master et al¹⁶ attached little prognostic significance to the localization of the infarct

Persistent sinus tachycardia, which occurred in 16 cases, was seen twice as often in the fatal (11 cases) as in the nonfatal (5 cases) Nodal tachycardia appeared in 2 cases, both fatal Auricular extrasystoles were present in 6 fatal and 7 nonfatal cases Ventricular extrasystoles appeared in 15 nonfatal and 9 fatal cases Auricular flutter was noted in 3 cases, all nonfatal Auricular fibrillation appeared in 7 fatal and 3 nonfatal cases Auriculo-ventricular block was found in 2 fatal and 4 nonfatal cases Left bundle-branch block was present in 15 cases, 6 nonfatal and 9 fatal, 5 cases showed incomplete and 10 complete block Right bundle-branch block and unclassified bundle-branch block occurred in 1 case each The mortality was significantly higher in patients showing complete than in those showing incomplete block

At the end of a month after the initial attack all electrocardiograms that had shown acute changes continued to show residua, this was also true of the three-month follow-up By the sixth month 9, at the end of the first year 15, at eighteen months 21, and at the end of two years 38 per cent of the electrocardiograms had reverted to normal

In the series of Master et al¹⁷ the electrocardiogram was normal in 21 per cent of cases within a year of the attack The absence of typical electrocardiographic changes in the follow-up period is well discussed by Sussman and Dack¹⁸ and by Parkinson and Bedford¹⁹

In the recurrent cases, both fatal and nonfatal, electrocardiographic residua persisted in all but 1 There was no predominance of anterior over posterior type or evidence of the type of occlusion to be expected following the initial attack Bundle-branch block was present in 4 of the 8 patients who developed fatal recurrences within a year No other constant finding was present The prognosis was found to be better if the changes were slight Recurrence was rare in patients with normal electrocardiograms

CLINICAL COURSE

Congestive failure was the most frequent condition complicating the hospital course Thirty-three per cent of the patients either had such failure on admission or developed it while hospitalized Fifteen per cent were admitted with failure already present, and 18 per cent developed it after admission

In the fatal cases 10 patients (30 per cent) had cardiac failure on admission, and 12 (35 per cent) developed failure during the hospital course—a total of 22 cases, or 65 per cent Woods and Barnes,⁷ Levine,³ Rathe,⁴ and Falk²⁰ stress the frequency of congestive failure in fatal cases In the nonfatal cases, 16 patients (25 per cent) either had decompensation on admission or developed it subsequently In Rathe's⁴ series decompensation occurred in 20.2 per cent

Seventy-nine per cent of all patients had pain on admission, but intractable pain persisted in only 16 per cent Such pain occurred in over 25 per cent of fatal and in only 10 per cent of nonfatal cases Although no reference was found in the literature to the relation of persistence of pain to prognosis, the incidence in this series is significant.

Of the 6 patients admitted with auricular fibrillation, 4 died and 2 survived This condition developed during the hospital course in 4 other cases, 2 of which were fatal Fibrillation persisted until death in all fatal cases but stopped either spontaneously or following medication in all surviving patients Askey and Neurath²¹ pointed out that the prognosis is poor in patients with persistent fibrillation, they found this condition in 1 in every 12 cases as a complication of acute myocardial infarction Fibrillation was present at some time in 10 per cent of the present series

Pericarditis, as manifested by a friction rub with or without pain, occurred in 10 per cent of the cases, 7 of which were fatal Rathe⁴ found pericarditis in 10 per cent of his cases Pericardial friction rubs were reported by Shillito et al¹ in 20 per cent of their cases, and by Blumer²² in 21 per cent

Bronchopneumonia occurred in 3 fatal and 4 nonfatal cases Coma occurred in 6, all of which were early fatal cases Pulmonary embolism occurred in 5 per cent, none of them fatal In Falk's²⁰ series massive pulmonary embolism was given as one of the chief causes of death in coronary occlusion A review of the autopsies in the present series, however, revealed only 1 case of pulmonary embolism Cerebral hemorrhage occurred in 1 fatal and 1 nonfatal case

In the fatal cases the average duration of life was eleven days after the onset of acute symptoms and seven days after hospitalization, the survivors were usually admitted earlier—on the average, three days after onset of the symptoms Hospitalization was generally for six or seven weeks

FOLLOW-UP STUDIES

Of the original 100 patients, 66 survived the initial attack and 58 were alive at the end of a year Seventeen patients had recurrences within a year, 8 of which were fatal Forty-nine patients had no recurrences within this period Patients who died of recurrences within a year were older than those who survived, and those who had nonfatal recur-

rences within this period were older (fifty-nine years) than those who had no recurrences (fifty-seven years). Men appeared more susceptible to fatal recurrence than women. The number of recurrences varied between one and three, the majority having only one in the period of observation.

The symptoms of cardiac decompensation were outstanding in the cases of fatal recurrence. Eighty-seven per cent were either on digitalis or had some symptoms of cardiac decompensation. Angina was present in only 50 per cent of this group.

In the cases of nonfatal recurrence angina was the outstanding symptom, being present in 88 per cent. Forty-four per cent of these patients either were on digitalis or had some symptom of cardiac insufficiency. Only 16 per cent of patients without recurrence either were on digitalis or had some symptom of cardiac insufficiency. Angina was present in approximately 50 per cent of these cases. Other complaints were infrequent, 22 per cent of these patients having no symptoms.

It is striking to note that the symptoms of cardiac insufficiency were most frequent among the fatally recurrent cases (75 per cent), much less frequent in patients who had nonfatal recurrences (33 per cent) and almost negligible in those who had no recurrence (8 per cent). Some degree of dyspnea was a fairly constant complaint in all three categories. Angina was more frequent in the cases of nonfatal recurrence than in either those of fatal recurrence or those of nonrecurrence.

In more than 50 per cent of Rathe's⁴ late fatal cases the patient had congestive heart failure, of the survivors only 20 per cent had this condition. In Bland and White's⁷ ten-year follow-up study, of the 30 per cent who survived 33.3 per cent had complete recovery, 33.3 per cent had angina, and 33.3 per cent had dyspnea.

No correlation could be made between the severity of the symptoms in the initial attack and the number of recurrent attacks, except for the cases of cardiac decompensation. The severity of the symptoms did not increase with the recurrences, whereas the incidence of decompensation did increase, and the prognosis was worse for those who had this condition. Decompensation, which was often not present during the first attack, usually appeared during the second.

Over 50 per cent of the patients who survived a year, with or without recurrence, were working, either full or part time. This percentage is lower than that given by Cooksey,⁵ who found that more than 75 per cent of the survivors returned to a useful occupation. Master et al,¹⁷ in a series of 202 cases, reported that 50 per cent of the survivors were able to return to work.

AUTOPSY FINDINGS

The results of autopsy were reported in 18 cases, 15 in the initially fatal and 3 in the recurrent group.

In all cases there was evidence of acute myocardial infarction, with the exception of 1 case in which a healed infarction was found. Sixteen cases showed definite evidence of coronary occlusion. In only 1 case was there evidence of occlusion of both arteries. The left coronary artery was involved in 62 and the right in 38 per cent.

In Baer and Frankel's¹⁵ series 70 per cent showed anterior, 23 per cent posterior, and 7 per cent antero-posterior occlusion.

Mural thrombus, ruptured posterior wall of right ventricle, aneurysm of left ventricle and interventricular septum, pericarditis and pulmonary embolism were found in 1 case each. In no case did autopsy show the gall bladder to be involved, although 3 patients had complained of gall-bladder symptoms during life.

SUMMARY AND CONCLUSIONS

Clinical observations in 100 cases of acute myocardial infarction are presented.

The older the patient at the time of the initial attack, the more serious the prognosis. The incidence was higher among men than among women, but mortality was higher among women, whose attacks tended to occur later in life.

In patients who gave a past history of cardiac decompensation the mortality was higher. The long-standing presence of angina or dyspnea had no particular influence on the prognosis.

Although pain was an outstanding chief complaint, it was not present in 21 per cent of the cases. In the fatal cases only 25 per cent of patients had severe precordial pain. Excruciating precordial pain, if not intractable, did not carry a poor prognosis, intractable precordial pain and epigastric pain occurred often in the fatal cases. Radiation of pain had no relation to mortality.

The symptoms of excessive dyspnea, orthopnea, nausea, vomiting, excessive fatigue or weakness were found in over half the initially fatal cases. Such symptoms appeared to be more significant than pain in the immediate prognosis.

The physical findings of edema, enlarged liver, ascites and disturbances of rhythm carried a poor prognosis. Fever and tachycardia were always present in the initially fatal cases.

The incidence of hypertension was greater in patients with coronary occlusions (74 per cent) than in the general population. There was no correlation, however, between antecedent hypertension and mortality rate.

The sedimentation rate, which was of help in establishing the diagnosis, was elevated in 90 per cent of cases. The height of the sedimentation rate, however, bore no relation to the prognosis. The white-cell count, which was of help in both diagnosis and prognosis, was elevated in 90 per cent of the initially fatal and in 70 per cent of the non-fatal cases. With counts between 20,000 and 25,000

cases were of the anterior variety. Levine and Rosenbaum¹⁴ noted that anterior infarction was more frequent in the initial attack than later. In Baer and Frankel's cases¹⁵ 52 per cent were of the anterior and 34 per cent of the posterior type. Rathe⁴ observed a definite predominance of anterior and indeterminate electrocardiographic patterns in early fatal cases. Willius⁸ and Master et al¹⁶ attached little prognostic significance to the localization of the infarct.

Persistent sinus tachycardia, which occurred in 16 cases, was seen twice as often in the fatal (11 cases) as in the nonfatal (5 cases). Nodal tachycardia appeared in 2 cases, both fatal. Auricular extrasystoles were present in 6 fatal and 7 nonfatal cases. Ventricular extrasystoles appeared in 15 nonfatal and 9 fatal cases. Auricular flutter was noted in 3 cases, all nonfatal. Auricular fibrillation appeared in 7 fatal and 3 nonfatal cases. Auriculo-ventricular block was found in 2 fatal and 4 nonfatal cases. Left bundle-branch block was present in 15 cases, 6 nonfatal and 9 fatal, 5 cases showed incomplete and 10 complete block. Right bundle-branch block and unclassified bundle-branch block occurred in 1 case each. The mortality was significantly higher in patients showing complete than in those showing incomplete block.

At the end of a month after the initial attack all electrocardiograms that had shown acute changes continued to show residua, this was also true of the three-month follow-up. By the sixth month 9, at the end of the first year 15, at eighteen months 21, and at the end of two years 38 per cent of the electrocardiograms had reverted to normal.

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In the recurrent cases, both fatal and nonfatal, electrocardiographic residua persisted in all but 1. There was no predominance of anterior over posterior type or evidence of the type of occlusion to be expected following the initial attack. Bundle-branch block was present in 4 of the 8 patients who developed fatal recurrences within a year. No other constant finding was present. The prognosis was found to be better if the changes were slight. Recurrence was rare in patients with normal electrocardiograms.

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Congestive failure was the most frequent condition complicating the hospital course. Thirty-three per cent of the patients either had such failure on admission or developed it while hospitalized. Fifteen per cent were admitted with failure already present, and 18 per cent developed it after admission.

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Bronchopneumonia occurred in 3 fatal and 4 nonfatal cases. Coma occurred in 6, all of which were early fatal cases. Pulmonary embolism occurred in 5 per cent, none of them fatal. In Falk's²⁰ series massive pulmonary embolism was given as one of the chief causes of death in coronary occlusion. A review of the autopsies in the present series, however, revealed only 1 case of pulmonary embolism. Cerebral hemorrhage occurred in 1 fatal and 1 nonfatal case.

In the fatal cases the average duration of life was eleven days after the onset of acute symptoms and seven days after hospitalization, the survivors were usually admitted earlier—on the average, three days after onset of the symptoms. Hospitalization was generally for six or seven weeks.

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USE OF SULFADIAZINE IN PRESENCE OF HEMATURIA

MAJOR JOSEPH H NICHOLSON, M C , A U S

IT is the purpose of this paper to discuss the renal reactions that occur after administration of sulfadiazine and to determine whether the clinical criteria generally accepted as indications for discontinuance of the drug are justifiable

The principal toxic reaction to sulfadiazine is renal irritation. Plummer and Wheeler¹ reported that of 705 patients receiving 2 to 4 gm initially, followed by 1 gm every four hours for not less than two and not more than fourteen days, 8 per cent showed definite evidence of toxicity to sulfadiazine, and that 48 per cent had renal irritation. Thus, more than half the cases of toxicity to the drug were due to renal irritation. Of 244 patients given one or more intravenous injections of sodium sulfadiazine, 12.3 per cent had some form of reaction and renal reactions occurred in 7.4 per cent. Thus, with intravenous sodium sulfadiazine, the incidence of renal reaction was almost doubled. It was also shown that the incidence of toxicity was generally in direct proportion to the concentration of sulfadiazine in the blood.

Disturbance of renal function resulting from sulfonamides has been well classified by Murphy et al.² into two types, the first of which comprises mechanical complications produced by masses of crystals of the sulfonamide compounds in the kidney tubules, pelves and ureters. This type may be further subdivided into the extraneuphric, in which the concretions causing obstruction are within the pelves of the kidneys or in the ureters, and the intraneuphric, in which the concretions are in the kidney substance itself. The second category includes toxic intrarenal lesions without mechanical obstruction. Such lesions occur within the kidney and may be attributed to the toxic effect of the sulfonamide compound on the parenchymal tissues. This class may be divided into three groups representing different phases of the same reaction and not distinct divisions — simple tubular degeneration, necrotic tubular degeneration and glomerular changes. In some cases there is evidence of obstructive and toxic parenchymal changes in the same kidney.

This brings up the question of the clinical manifestations that are indications for the discontinuance of sulfadiazine. The urinary reactions to sulfadiazine are microscopic hematuria, gross hematuria, renal pain (usually pain similar to that in renal infarction and typical ureteral colic), oliguria and anuria. There is divided opinion regarding which of these conditions demand discontinuance of the

drug. The appearance of microscopic or macroscopic hematuria, renal colic or anuria has been held to be a definite indication for stoppage of the drug.^{3,4} On the other hand, microscopic hematuria⁵ and ureteral colic⁶ have not been considered definite contraindications to its continuation.

In an attempt to determine just what clinical criteria should be used in ascertaining whether the drug should be discontinued in the presence of renal complication resulting from sulfadiazine therapy, the renal reactions resulting from such therapy on the meningitis service of the Fort McClellan Regional General Hospital were reviewed.

The incidence of urinary complications is generally quite high in patients with meningococcal meningitis or meningococcemia, the reported percentages varying from 5 to about 26 in large groups of patients.⁵⁻⁸ This incidence would be lower if microscopic hematuria were not considered a complication. In smaller series no renal reactions were encountered.⁹

At this hospital all patients with meningococcal infections are given an initial oral dose of 4 gm of sulfadiazine, followed by 2 gm every four hours. Frequently, oral administration is not possible because of vomiting or because of the semistuporous and maniacal condition of the patient. In such cases, an initial intravenous dose of 5 gm of sodium sulfadiazine is given, followed by repeated intravenous injections in doses of 2.5 or 5.0 gm, the amount depending on the blood level, which is maintained at 10 to 15 mg per 100 cc. In some cases it was impossible to maintain an adequate blood level by oral administration, but with improvement in the patient's general condition adequate blood levels were easily maintained. When oral administration was not possible intravenous sodium sulfadiazine was given. As pointed out by other observers,¹⁰ marked and unpredictable variations in blood sulfadiazine concentration followed both intravenous injection and oral administration, although fluctuations were generally less marked with the latter route. This fact emphasizes what has often been stated, namely, that frequent determinations of the blood level are essential. During the first twenty-four hours, 10 to 20 gm of sodium sulfadiazine was frequently given intravenously, and as much as 50 gm within a period of three days.

Recently alkalies have been advocated as adjuvants to sulfadiazine. It has been shown that with an alkaline urine the solubility of both free and acetylated sulfadiazine crystals is markedly increased.¹⁰ The recommendation has been made that

the prognosis was grave, but with those above 25,000 the mortality was 100 per cent

Electrocardiographic evidence of involvement of the left coronary artery was more frequent (52 per cent) than that of the right coronary artery (40 per cent), and the mortality was higher in patients with the former. Persistent sinus tachycardia, auricular fibrillation and complete bundle-branch block carried a grave prognosis. Stabilization of the electrocardiogram following the acute changes occurred by the beginning of the third week. Persistence of residua in the follow-up electrocardiograms was more frequent in the recurrent than in the nonrecurrent cases. There was no recurrence in cases in which the electrocardiograms reverted to normal.

Cardiac decompensation developed during the hospital course in over half the fatal cases and in less than one fifth the nonfatal cases. Patients who developed the signs of pericarditis had a high mortality, those who were admitted in coma or who went into coma died.

The older the patient at the time of the initial attack, the greater the likelihood of recurrence. Men succumbed to recurrences oftener than women. Cardiac decompensation was more frequent in patients with either fatal (87 per cent) or nonfatal (47 per cent) recurrences.

Findings at autopsy confirmed the predominance of involvement of the left (62 per cent) over that of the right coronary artery (38 per cent) shown by electrocardiogram.

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a solution has an alkalinizing effect in the body equivalent to an oral dosage of 15 gm of sodium bicarbonate, and 1000 to 1500 cc renders the urine alkaline in patients with acidosis from acute infections. Once the urine is alkaline a total daily dosage of 1100 cc of one-sixth molar sodium lactate solution, given in two twelve-hour injections, is sufficient to maintain alkalinity. It is reported that with this solution practically no renal irritations followed intravenous administration of sodium sulfadiazine.¹¹

In this series of patients adequate hydration and alkalinization of the urine was obtained by the administration of at least 3000 cc of fluids and by the use of alkalis. Twelve to 20 gm of sodium bicarbonate was given orally in repeated equal doses every four hours. In the majority of cases 15 gm, divided into 2 5-gm doses, was given every

four hours. In distilled water it was immediately followed by either Hartman's or Ringer's solution in doses of 1000 or 1500 cc. In some cases 5 per cent glucose in normal saline solution was given.

Group 2 included 18 cases with similar diagnoses in which one-sixth molar solution of sodium lactate was used instead of Hartman's solution. In these cases, the sodium sulfadiazine was dissolved in the lactate solution to make a 1 per cent solution and was given intravenously. Generally no more than 2000 cc of one-sixth molar solution of sodium lactate was given in a twenty-four-hour period.

In Group 1 there were renal reactions in 12 cases, 4 showing microscopic and 8 gross hematuria (Table 1). In Group 2 there were 2 cases of gross hematuria (Table 2).

A record of the fluid intake and output was not obtained in all cases. Charts had been kept at the

TABLE 2 Data on 2 Patients with Meningitis Treated with Sodium Sulfadiazine in Combination with One-Sixth Molar Solution of Sodium Lactate

CASE No	DAY OF THERAPY	URINARY FINDINGS		AMOUNT OF SULFADIAZINE ADMINISTERED		BLOOD SULFADIAZINE LEVEL	FLUID INTAKE	FLUID OUTPUT
		REACTION	ALBUMIN	SEDIMENT*	INTRA-VENOUSLY			
		pH			gm	mg/100 cc	cc	cc
1	1	Not recorded	0	Negative	15.0	6	10.4	4750
	2	7.5	0	Negative	2.5	12	13.3	3650
	3	7.5	—	Gross blood	0	12	12.7	4100
	4	7.5	++	100-125 red cells	0	12	12.3	3600
	5	7.5	0	Negative	0	12	10.6	2400
	6	7.5	0	Negative	0	12	Not recorded	—
	7	7.5	0	Negative	0	12	11.4	—
	8	Not recorded	0	Negative	0	12	Not recorded	—
2	1	6.5	0	2-3 white cells	7.5	7	13.6	2220
	2	7.5	++	Gross blood	0	14	9.1	2840
	3	7.5	++	Gross blood	0	6	17.4	4820
	4	7.5	0	1 red cell	0	6	9.7	4800
	5	7.5	0	Negative	0	6	9.7	4560

*Numbers refer to those seen per high power field

four hours. When patients were unable to take or retain anything by mouth, fluids were given intravenously. The alkalinity of the urine was generally maintained at pH 7.5 or higher, each specimen being tested with nitrazine paper to determine its reaction. When it was below pH 7.5, either Hartman's solution or one-sixth molar sodium lactate solution was given intravenously, or the amount of sodium bicarbonate was increased.

The laboratory findings in the cases in which renal reactions occurred during sulfadiazine therapy are presented in Tables 1 and 2. These cases were divided into groups.

Group 1 included the renal reactions occurring in a study of 50 cases of meningococcal meningitis and meningococcemia in which alkalinization was carried out by the use of sodium bicarbonate in the doses described above when oral medication was possible, and by the use of Hartman's solution when oral medication was impossible. When intravenous sodium sulfadiazine was given in a 5 per cent solu-

tion in distilled water it was immediately followed by either Hartman's or Ringer's solution in doses of 1000 or 1500 cc. In some cases 5 per cent glucose in normal saline solution was given.

Three of 4 cases with microscopic hematuria had a urinary alkalinity of pH 7.5, and in 6 of 10 cases with gross hematuria the reaction was pH 7.5.

In no case was the sulfadiazine stopped because of hematuria, either microscopic or macroscopic, and in all cases the urinary output was adequate. If the urine was not alkaline, attempts were made to render it so, either by an increase in the dose of sodium bicarbonate or by the administration of Hartman's or Ringer's solution. In cases in which one-sixth molar solution of sodium lactate was used the urinary reaction was always alkaline. When hematuria occurred in both groups an additional 1000 cc of Hartman's, Ringer's or one-sixth molar lactate solution was given intravenously.

15 gm of sodium bicarbonate, or various amounts of other sodium salts with equivalent available base excess, be given daily in divided doses of 2.5 gm

tract obstruction was encountered during treatment with sulfadiazine orally or with sodium sulfadiazine intravenously¹ More recently, one-sixth molar

TABLE 1 Data on 12 Patients with Meningitis Treated with Sodium Sulfadiazine in Combination with Sodium Bicarbonate or Hartman's Solution

CASE No	DAY OF THERAPY	URINARY FINDINGS			AMOUNT OF SULFADIAZINE ADMINISTERED		BLOOD SULFADIAZINE LEVEL	FLUID INTAKE	FLUID OUTPUT
		REACTION	ALBUMIN	SEDIMENT*	INTRAVENOUSLY	ORALLY			
		pH			gm	gm	mg/100 cc	cc	cc
1	1	6.5	0	3-4 white cells	11	0	—	—	—
	2	7.5	+	10-15 red cells	3	18	12.2	—	—
	3	7.5	+	25-30 red cells	0	10	11.9	—	—
	4	7.5	0	Negative	0	6	11.9	—	—
2	1	5.5	0	—	10	2	13.8	3690	1140
	2	7.5	++	5-10 red cells	7.5	8	8.7	3270	2500
	3	7.5	++	40-50 red cells	0	12	12.7	4500	3360
	4	7.5	+	25-30 red cells	0	12	9.3	3120	3100
	5	7.5	0	Negative	0	12	17.6	3240	2160
3	1	7.5	0	2-3 white cells	10	13	12.0	—	—
	2	7.5	0	Rare red cells	0	6	14.6	—	—
	3	7.0	++	15-20 red cells and many sulfadiazine crystals	0	6	14.1	—	—
4	4	6.5	+	Rare red cells	0	6	10.5	—	—
	1	6.0	+	3-4 white cells	5	16	—	—	—
	2	6.0	+	1-5 white cells	0	12	—	—	—
	3	7.5	++	35-40 red cells	0	6	—	—	—
	4	7.5	0	Negative	0	6	—	—	—
5	5	7.5	0	Negative	0	6	—	—	—
	1	5.5	0	—	10	5	—	4200	1140+
	2	5.5	++	Gross blood	0	12	12.4	—	—
	3	7.0	+	8-10 red cells	5	18	7.7-17.5	—	—
	4	7.0	+	Negative	0	16	12.9	—	—
	5	5.5	—	25-40 red cells	0	7	15.2	—	—
	6	7.5	0	—	0	6	8.1	—	—
6	7	7.5	0	—	0	6	6.4	—	—
	1	7.0	0	Rare white cells	0	14	9.0	—	—
	2	7.0	0	Negative	0	9	6.5	—	—
	3	7.5	0	Negative	5	12	6.0	—	—
	4	7.5	++	Gross blood	0	12	12.8	—	—
	5	7.5	0	Negative	0	7	10.0	—	—
	6	6.5	0	Negative	0	6	7.3	—	—
7	7	5.5	0	Negative	0	0	—	—	—
	1	6.5	0	Negative	5	5	—	—	—
	2	7.0	++	Gross blood	0	6	12.7	—	—
	3	7.5	+	Red cells	0	6	7.1	—	—
	4	7.5	0	—	0	6	7.5	—	—
8	5	7.5	0	—	0	6	—	—	—
	1	Normal	0	1-2 red cells	5	11	—	—	—
	2	6.0	+	1-2 red cells	5	6	7.5	—	—
	3	7.5	++	Gross blood	0	6	6.5	—	—
	4	7.5	+	5-6 red cells	0	6	9.7	—	—
	5	7.5	+	5-6 red cells	0	6	10.0	—	—
	6	7.5	0	Negative	0	6	10.0	—	—
9	7	7.5	0	Negative	—	—	—	—	—
	1	7.0	0	Negative	13	0	15.4	5750	1980
	2	7.5	+	Gross blood	3	11	11.3	4000	3360
	3	7.5	++	Gross blood	0	8	11.7	5680	2250
	4	7.5	0	Negative	0	6	12.0	3760	2640
	5	7.5	0	Negative	0	12	7.5	4100	3050
	6	7.5	0	Negative	0	12	8.3	3000	2820
	7	7.5	0	Negative	0	9	12.0	3120	3300
	8	7.5	0	Negative	0	6	12.2	4200	—
10	9	7.5	0	Negative	—	—	—	7797	2950
	1	5.0	++	Hyaline and granular casts	—	—	25.3	5900	2760
	2	6.5	++	Gross blood	0	7	15.7	4000	—
	3	7.5	+	4-5 red cells	0	6	8.5	—	—
	4	7.5	0	Negative	0	6	8.8	—	—
	5	7.5	0	Negative	0	6	8.8	—	—
	6	7.5	0	Negative	0	6	8.5	—	—
11	7	7.5	0	Negative	0	6	—	3100	1050
	1	5.5	0	Negative	10	3	8.3	—	—
	2	7.5	0	Negative	7.5	4	9.3	—	—
	3	7.5	++	Gross blood	2	6	12.0	3120	2500
	4	7.5	++	Gross blood	0	7	7.0	3840	3000
	5	7.0	++	Gross blood	0	6	12.0	5420	4620
	6	7.5	++	Gross blood	0	6	10.0	4600	4000
	7	7.5	+	40-50 red cells	0	6	9.2	4320	3310
	8	7.5	0	Negative	0	6	9.7	2400	2500
12	9	—	0	Negative	0	6	9.2	3420	2820
	1	5.5	++	Gross blood	10	6	10.9	—	—
	2	5.5	++	Gross blood	2.5	12	10.7	5040	3660
	3	6.5	++	Gross blood	0	12	12.0	4320	2520
	4	7.5	+	15-20 red cells	0	12	—	—	—
	5	7.5	0	Negative	0	12	12.1	—	—
	6	7.5	0	Negative	0	12	—	—	—
	7	7.5	0	Negative	0	12	15.3	—	—

*Numbers refer to those seen per high power field

every four hours. In the treatment of approximately 200 patients whose urine was kept alkaline or neutral, no evidence of renal irritation or urinary-

sodium lactate solution has been administered parenterally to alkalinize the urine when sodium sulfadiazine was given parenterally, 1100 cc of such

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THE USE OF ETHER IN THE NARCOANALYSIS OF PATIENTS
WITH WAR NEUROSES

HENRY H BREWSTER, M D *

PHILADELPHIA

THIS report deals with the technic and utility of ether in the treatment of war neuroses. Comparing ether to Pentothal, as used by Grinker and Spiegel,¹ Sargant and Shorvon² and Kelley³ found the former more effective for ventilating repressed emotions in acute war neuroses. That ether is useful in psychotherapy for other reasons is suggested by Sargant and Shorvon and also by Rogerson⁴ in his account of nitrous oxide narcoanalysis of civilian patients with acute and chronic anxiety. Between January and May, 1945, ether was used at the 5th General Hospital in France in the psychotherapy of 100 neuropsychiatric patients. To comprehend the particular usefulness of ether one must understand the local problem of psychotherapy that existed at the hospital. The patients treated were, in general, combat soldiers who had been evacuated from the front for psychiatric reasons and who had spent from two to six weeks in other hospitals en route. In some cases Pentothal had been used at the forward hospitals, in others, the patients had received sedation and rest. On arrival at the 5th General Hospital, the patient usually presented a combination of certain persistent symptoms, such as anxiety and tremulousness, sensitivity to noise, anorexia, recurrent terrifying dreams and insomnia, irritability and, often, a generalized headache. In a small number of cases aphonia, weakness of the legs and other grossly hysterical symptoms were present, without external evidence of anxiety. The selected patient received a two-week program of treatment. A medical examination was completed, and a brief psychiatric history was taken, with special attention to the circumstances immediately preceding the patient's psychiatric breakdown as well as to the content of his dreams, both of which supplied starting points for an ether interview. On the day after admission to the hospital,

the patient received an ether interview, which was followed by two days of light sedation† during the afternoon and night and insulin therapy‡ in the morning. During the next three days the patient received insulin in the morning and group psychotherapy and physical exercises in the afternoon. After this period of treatment, he was transferred to a reconditioning company separated from the other hospital patients and under the command of a nonmedical officer, where he lived the life of a garrison infantry company and was assigned to duties necessary to the running of a hospital and peculiar to his own ability. After ten such days in the reconditioning company the patient was interviewed and re-evaluated by the psychiatrist. The ether examinations were done in a semi-darkened room. The patient was told in the morning that he would be interviewed in the afternoon with the aid of some medicine that would make it easy for him to talk about his experiences. In preparation for ether he received no food for six hours and 0.6 mg of atropine sulfate subcutaneously half an hour before the interview. None of the major complications of ether administration occurred. It should be noted that patients as a rule did not receive sedation preceding the interview, in 5 patients who had received sodium amytal the day before the interview, only an ineffective emotional response could be obtained under ether. Ether was administered by the open-drop method by a trained anesthetist. The patient was prompted by the psychiatrist to relate in chronologic order the events leading up to his psychiatric difficulties. Within two to five minutes the patient reached a mental state in which he was reliving his painful battlefield experience and expressing the emotion

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†After lunch 0.4 gm sodium amytal was given by mouth, and after supper 0.6 to 0.8 gm.

‡About 50 units of regular insulin was injected subcutaneously at 10:00 a.m. producing mild symptoms of hypoglycemia which were relieved by a high-calorie lunch at 12:00 p.m. The insulin therapy generally increased the patient's appetite, caused him to gain weight and reduced to a minimum the hangover associated with the use of sodium amytal.

DISCUSSION

In these 14 cases of renal irritation occurring during sulfadiazine therapy for meningococcal infections, 4 patients had microscopic and 10 gross hematuria. In spite of the hematuria, continuation of sulfadiazine therapy had no untoward effects, and in all cases the urine returned to normal. Such continuation of the drug in the presence of hematuria, particularly gross hematuria, is in disagreement with generally accepted procedure and calls for evaluation. Many cases of renal reaction from sulfadiazine, some fatal and others requiring either drastic treatment, such as ureteral and pelvic lavage and nephrostomy, have been reported in the literature.¹²⁻²⁰

In all the cases reported in the literature the urinary output varied from definitely diminished to absent, and alkalinization of the urine was not attempted or was inadequate. Fox et al.²¹ have pointed out the value of alkali therapy in the prevention of renal reactions, as well as the fact that adequate doses of alkalis must be given and that the required quantity of alkalis must be governed primarily by the reaction of the urine.

In spite of alkalinization of the urine, however, renal reactions from sulfadiazine occurred in the cases discussed above. To afford a good method of comparison, there is available the incidence of renal reactions at this hospital prior to the use of alkalis as adjunctive therapy, as reported by Marangoni and D'Agati.⁶ In 46 cases of meningococcal infection in which both oral and intravenous sulfadiazine were given 26 per cent of patients showed toxic renal reactions. This was only a slightly higher incidence than that in cases in which oral sulfadiazine was used alone. But the dosage was larger than that ordinarily given, with blood sulfadiazine levels of 15 to 20 mg per 100 cc. In a similar group of patients with alkaline urine, as reported above, there were renal reactions in approximately 13 per cent. This is an appreciable lowering of rate but is not in accord with other observations that alkalinization of the urine will check renal reactions. In none of the cases discussed above was there definite evidence of diminished urinary excretion or of renal colic, although renal colic may have been present in some cases for a fair percentage of the patients were semistuporous and disoriented and were therefore not easily observed, conscious and rational patients, however, gave no complaint that might have been interpreted as renal colic.

The renal irritation resulting from the use of sulfonamides is described above. Plummer and Wheeler,¹ however, in autopsies on 6 patients with renal irritation during sulfadiazine therapy who died of other causes, found concretions of the drug in the renal pelvis and deposits of the drug within the renal parenchyma, with tubular degeneration and interstitial inflammatory reaction and occasional

secondary degeneration of the nephron, they believed that no permanent or serious impairment of renal function would have ensued in the patients examined.

The factors that might be expected to influence the occurrence of renal reactions from sulfadiazine are the total dosage of the drug and the route of administration, the fluid balance, the reaction of the urine and individual sensitivity to the drug.

Most renal reactions occurring during sulfadiazine therapy are due to mechanical complications resulting from crystallization in the substance and pelvis of the kidneys and in the ureters. Clinically, however, renal irritations due to mechanical complication and those caused by the toxic effect of the drug on the kidneys cannot always be differentiated. The presence of renal or ureteral colic and crystal linuria suggests mechanical complications, but such symptoms and findings may be absent and the only sign may be hematuria, oliguria or anuria, even though concretions of sulfadiazine crystals are responsible for the renal reactions.

The most significant finding in renal reactions from sulfadiazine is not the presence of hematuria, with or without crystallinuria, but urinary output and alkalinity. If the urine is kept alkaline and fluid balance maintained, sulfadiazine can be continued, as in all the cases discussed above, which cleared without any evidence of residual damage.

CONCLUSION

Hematuria, either microscopic or macroscopic, is not a contraindication to continued use of sulfadiazine provided there is no diminished urinary output and provided the urine is kept alkaline and the fluid balance is maintained.

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sleepy or groggy and subsequently remember nothing of the interview. The clinical value of abreaction is lost if the patient has amnesia for the procedure,⁶ since the amnesia represents the same state of repressed emotions that existed preceding the interview. Finally, ether has a pharmacologic value: it is absorbed readily by the lungs, produces its clinical effect promptly, and is eliminated quickly and in large part by the lungs. Because of its rapid elimination it is possible to lighten the level of ether anesthesia speedily by controlling the quantity being given the patient; Pentothal does not have this advantage.

The ether interview provided a useful means of surveying the conflicts of a neurotic patient and selecting patients suitable for the two-week program of treatment, and was also useful in clarifying a diagnosis, as when a mute patient under ether appeared to suffer from a case of severe anxiety, hysteria or psychosis. Ether is contraindicated in severely agitated patients, however, in whom it may release a dangerous amount of anxiety.

Under the circumstances described above ether interviews were an adjunct in treatment of patients who had had little previous psychiatric difficulty but had developed moderate to severe anxiety during and after combat, and of those with hysteria. That ether was a significant factor in the therapeutic results obtained from the two-week treatment program outlined is suggested by the following statistics. Fifty neurotic patients received this two-week program of treatment except that the

ether interviews were omitted, only 2 of these patients were capable of resuming duty overseas. One hundred similar patients received the two-week program of treatment, including the ether interviews. Of these, 50 were satisfactorily performing noncombat duty overseas one and two months after discharge from the hospital.

SUMMARY

A technic of administering ether to the psychiatric patient is described.

Ether was found to have the following advantages: it produced an excessive emotional response and maintained a useful hypnotic state for abreaction.

An interview under ether was a quick and useful method of surveying the conflicts of neurotic patients coming to an Army general hospital from combat.

In the treatment of 100 such patients in France, selected for two weeks of psychotherapy, ether interviews were found to be a significant adjunct to treatment.

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associated with it. It was necessary for two to four attendants to restrain the patient during the excitement that generally occurred while he was reliving a traumatic incident. As soon as he had made the mental transition to a hypnotic state, ether administration was stopped. The patient subsequently remained in this state as long as the psychiatrist chose to maintain it. This allowed the psychiatrist to probe a traumatic incident, to recover the facts of the amnesic period frequent in such cases and to investigate the past history and its associated conflicts—in short, to abreact the patient at will and to the extent indicated. Occasionally the patient suddenly came out of the hypnotic state, and ether was readministered. In an hour's interview, it was sometimes necessary to administer ether once, twice or three times. The psychiatrist brought the patient out of the hypnotic state by reviewing chronologically the events leading up to admission to the hospital. Since the patient was conscious throughout the ether interview, he did not usually forget the material discussed during the abreaction.

Sometimes a patient is unduly slow in making the transition to the hypnotic mental state. When a patient who has been asked to narrate the events leading up to his mental breakdown begins to grow anxious or restless, the psychiatrist should intensify verbal, auditory or visual suggestion. Suddenly the patient talks in the present rather than the past tense, regards the psychiatrist as some person in his past experience, and is fully hypnotized. When difficulty is encountered in hypnosis particular factors should be considered. One is that the patient may be breathing with shallow respiration, making use only of his upper chest and thus indefinitely postponing the effect of the ether. To remedy the situation the psychiatrist should hold his hands against the lower lateral thorax and instruct the patient to take deep breaths, the patient thereby increases the excursion of respiration and inhales a larger quantity of ether.

Another factor to remember is that, during the ether induction, the psychiatrist may be suggesting to the patient a series of events that the psychiatrist thought, on eliciting the medical history, had been traumatic, but that actually had little emotional impact for the patient. For example, in giving his medical history preceding the ether interview, a patient states that he grew anxious during combat, that one day a shell burst near him and that he remembered nothing until he awoke in a hospital. The psychiatrist suggests these events during ether induction but finds that the mention of shellfire provokes little emotional response and that the patient remains un hypnotized. In that event, the psychiatrist should allow the patient to be etherized just short of unconsciousness and should then investigate further the medical history. Eventually he will discover the circumstances that are really

charged with emotion for the patient—a shell burst near him on the battlefield, he saw his buddy torn to shreds, he burst into tears and grew confused, and finally he was carried on a litter to a hospital, where his mental state was found to be anxious, agitated and disoriented. These remarks are most applicable to a chronic neurotic patient for whom combat experience has precipitated symptoms but for whom the conflicts of civilian life are associated with a far greater emotional charge. During the ether interview, such patients may well, by a process of free association, change their train of thought from combat experience to the more significant episodes of earlier life.

It should be borne in mind that in any patient aspiration of stomach contents and apnea may occur during ether anesthesia, but the chance is slight if the patient has fasted for six hours and has been atropinized. It should not be attempted if the patient has a pulmonary infection. The factor of safety is further increased if the anesthetist is experienced and an oxygen tank and mask are available.⁵ The complications mentioned above can develop quickly and unexpectedly and must be handled expeditiously and correctly. In general, however, ether is a safe drug for use in psychotherapy. Since it is absorbed and eliminated rapidly by the lungs, the level of anesthesia can be maintained easily and lowered more rapidly than that of intravenous drugs like Pentothal. It has been thought that the emotional excitement of patients during an ether interview is the same as that often seen in the surgical operating room during ether anesthesia. As Searles⁵ points out, however, the latter excitement occurs during the primary stage of ether anesthesia—a state during which, by definition, the patient is unconscious. During the psychiatric interview under ether, on the other hand, the patient is always conscious. Therefore the psychiatric patient must be in a stage just short of the accepted primary stage of ether anesthesia. During this preprimary stage, Searles believes that auditory stimuli are greatly exaggerated. Hence, the auditory suggestions made by the psychiatrist must be aggravated to a frightening degree by the action of ether. This observation may explain why ether seems to precipitate a greater emotional response than Pentothal, which is a sedative as well as an anesthetic.

Under the qualifying circumstances described above, ether presented several striking attributes in the treatment of combat neuroses. The most prominent was that in most cases it precipitated quickly an intense emotional response, which is a prerequisite for successful abreaction.⁶ A second attribute was that the ether produced a useful mental state for abreaction: the patient was conscious and alert during and after the interview, retaining a memory of what had transpired. Patients who have received Pentothal often grow

sleepy or groggy and subsequently remember nothing of the interview. The clinical value of abreaction is lost if the patient has amnesia for the procedure,⁶ since the amnesia represents the same state of repressed emotions that existed preceding the interview. Finally, ether has a pharmacologic value: it is absorbed readily by the lungs, produces its clinical effect promptly, and is eliminated quickly and in large part by the lungs. Because of its rapid elimination it is possible to lighten the level of ether anesthesia speedily by controlling the quantity being given the patient; Pentothal does not have this advantage.

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ENHANCING THE RIBOFLAVIN CONTENT OF MARE'S MILK*

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ALTHOUGH cow's milk is generally considered one of the best natural sources of riboflavin, Holmes and his co-workers,¹ in a study of the vitamin content of mare's milk, found that draft (Percheron) mares produced milk containing extremely little riboflavin. The riboflavin levels varied from 0.05 to 0.20 mg per liter of milk, with averages of 0.09, 0.11, and 0.13 mg for the three mares used in the study. These values were less than one tenth those found for milk produced by cows that grazed in the same pastures and were fed hay grown in the same or adjacent fields to those that provided hay for the mares. Whether this difference in the riboflavin content of milk is related to the type of digestive tract of the two species — the cow is a ruminant, whereas the mare is a nonruminant — or whether some other factor is responsible is not known. Bechdel and his co-workers² and McElroy and Goss³ demonstrated that cows synthesize vitamin B in the rumen. Wegner et al.⁴ and Hunt and his associates⁵ showed that these animals can synthesize riboflavin in the rumen. The amount that can be synthesized is influenced by the type of ration, corn being particularly favorable for the rumen synthesis of riboflavin. Since mares have no rumen, they cannot add to their milk riboflavin produced by this type of bacterial synthesis.

Until foals begin eating hay, grass and concentrates, the mare's milk is the total source of riboflavin. Hence, the low riboflavin content of mare's milk naturally raised a question concerning its adequacy for supplying the riboflavin requirements of rapidly growing foals. The literature that was consulted contained, however, no information concerning the riboflavin nutrition of young foals, and this study was undertaken to accumulate additional data regarding the possibility of increasing the riboflavin content of mare's milk by feeding crystalline riboflavin ‡

EXPERIMENTAL PROCEDURE

Three Percheron mares were available for this study. They were normal, active, well developed animals. Mare 1 was seven years old, weighed 1900 pounds and produced four foals, Mare 2 was fourteen years of age, weighed 1800 pounds and had produced ten foals, and Mare 3 was five years old, weighed 1430 pounds and had produced her first foal.

None of the mares had been harnessed since the last foals were born. Accordingly, their food was utilized solely for their and the foals' body needs.

The experiment with Mares 1 and 2 was conducted during the summer months. During the night the mares received pasturage of rapidly growing green grass. During the day they were confined in a cool, shaded barn away from flies. The daytime feeding consisted of good-quality July-30-cut hay, mixed timothy, alfalfa and clover, three or four quarts of crushed oats and six or eight medium-sized ears of well cured white dent corn. The experimental period for Mare 3 was late winter and early spring, and her ration consisted of the same amounts of crushed oats and whole corn, with all the hay she desired.

Since riboflavin is only slightly soluble in water, a large volume of water would have been required for dissolving appreciable amounts of riboflavin and it would have been difficult to administer large amounts of liquid quantitatively. Accordingly, it was decided to feed the riboflavin in dry form. Since horses are particularly fond of sugar, this was used as a base. To prevent undesirable separation, both the sugar and the riboflavin crystals were ground to 100-mesh fineness and intimately mixed. The mixture was placed in No. 2 hard gelatin capsules, which were one third the size of a kernel of corn and somewhat larger than a crushed oat kernel. Thus, the amount of riboflavin contained in an individual capsule was relatively small. The capsules were mixed with the crushed oats. The mares were watched while they consumed their grain, and all the animals ate all the capsules.

During the sixteen-day prefeeding period, no crystalline riboflavin was fed. At its termination, Mare 1 was in the twenty-third week and Mare 2 in the thirteenth week of lactation. The riboflavin-containing capsules were administered for the next twenty-two days. During the first eight days each mare received 140 mg of riboflavin daily, and for the next three days 160 mg. The amount was then increased to 350 mg daily for nine days, after which the supply of riboflavin was nearly exhausted, and only 315 mg was fed for the next two days. Thus, each mare received a total of 5.26 gm of crystalline riboflavin during the twenty-two-day feeding period. The prefeeding period was twenty-four days for Mare 3, at that time she was in the seventeenth week of lactation. She was fed 100 mg of riboflavin daily for fourteen days, and 200 mg for the next fourteen days, after which she was unexpectedly removed.

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‡The riboflavin was supplied through the courtesy of Dr. D. F. Green, Merck and Company, Incorporated, Rahway, New Jersey.

from the experiment and it was not possible to feed a larger amount or to assay her milk following the discontinuance of riboflavin feeding.

When the mares and foals were taken to the barn from the night pasture, they were separated. Two hours later milk was collected for riboflavin assay. During the early part of the study, even though the mares' udders contained milk after they had been separated from the foals, it was impossible to obtain any milk from them. Consequently, the foals were returned to their dams. As a result, the mares gave their milk and a sample was collected for assay while the foal was nursing. As the study progressed, the foals became less dependent on milk and the

four days, the riboflavin content of their milk suddenly increased to about four times that of the prefeeding period. In Mare 2, the maximum value was obtained on only one day, however, and the riboflavin content of the milk decreased day by day even before the riboflavin feeding was discontinued. The riboflavin content of the milk from Mare 1 likewise increased rapidly during the period of 350 mg daily, but this level was maintained so long as the maximum quantity of riboflavin was administered. Following the withdrawal of the crystalline riboflavin, the amount of riboflavin in the milk rapidly decreased, and when the fifty-four-day study was terminated, the riboflavin content of the milk of both mares had returned to the prefeeding level. During the prefeeding period the milk from Mare 3 averaged 0.13 mg per liter. The average for the fourteen days that she was fed 100 mg of riboflavin daily was 0.22 mg, and while she was fed 200 mg, 0.20 mg per liter. Since the experiment was unavoidably terminated at this point, no data were collected concerning the riboflavin content of the milk following riboflavin feeding.

Discussion

The data obtained in this study revealed that it was possible to increase the riboflavin content of milk from draft mares by feeding large amounts of crystalline riboflavin, but the increase was of short duration and the amount in the milk rapidly returned to normal levels. It is evident from these observations that the oral administration of riboflavin to mares is not an efficient method of increasing the foals' intake of riboflavin. Instead, natural riboflavin can be administered by feeding the foal as much skimmed cow's milk as it will consume.

In considering the low efficiency in supplying riboflavin to the foal through feeding crystalline riboflavin to the mare, it is interesting to note some of the results obtained by investigators who fed large amounts of vitamin A to animals or human subjects. Deuel and his associates⁷ succeeded in materially increasing the vitamin A content of milk from Holstein and Guernsey cows by feeding large amounts of vitamin A (shark-liver oil). In a later study, Hrubetz, Deuel and Hanley⁸ obtained a 200 per cent increase in the vitamin A content of human milk by feeding 100,000 international units of vitamin A per day to women from the sixth month of pregnancy to the termination of lactation, and the high level of vitamin A was maintained throughout lactation. In the present study, the increased riboflavin content of the mare's milk was extremely transient, but it could possibly have been maintained if massive doses of riboflavin had been administered throughout lactation. No information, however, is available concerning the requirements of young foals for riboflavin, even though Pearson, Sheybani and Schmidt⁹ state that riboflavin is a dietary essential for the horse, and Jones¹⁰ and Jones, Maurer and Roby¹¹ report

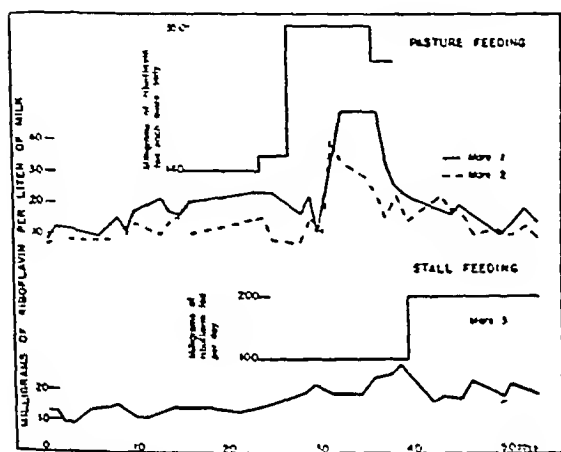


FIGURE 1 Effect of Feeding Riboflavin on Its Presence in Mare's Milk

mares became more accustomed to the procedure and could be milked satisfactorily while the foals were separated from them. As soon as the sample was collected, it was taken directly to the laboratory, where riboflavin assays were started at once without the milk's being cooled. As is obvious, the quantity of milk available for analysis did not represent twenty-four-hour samples.

The riboflavin assay was conducted by the fluorometric method described by Holmes and Jones⁶ for the assay of cow's milk.

RESULTS

The effect of the administration of crystalline riboflavin on the riboflavin content of mare's milk is shown graphically in Figure 1. The riboflavin content of the samples of milk obtained from each mare varied from day to day. During the prefeeding period, the riboflavin content averaged 0.13 mg per liter for Mare 1 and 0.09 mg for Mare 2. During the period in which the mares received 140 or 160 mg of riboflavin daily, there was little increase in the riboflavin content. In contrast, after the mares had been receiving 350 mg of riboflavin daily for

that ophthalmia and other deficiency symptoms develop when horses are fed riboflavin-deficient rations for considerable periods

SUMMARY

The average riboflavin content of milk from two normal draft mares was determined for a fourteen-day pre-experimental period. Subsequently, a total 5.26 gm of crystalline riboflavin was administered to each mare during a twenty-two-day feeding period. The riboflavin content of the milk increased about fourfold, but the increase was of short duration and the content soon returned to the pre-experimental level. When a third mare was fed 100 mg of riboflavin daily for fourteen days, the riboflavin content of the milk increased from 0.13 mg to 0.22 mg per liter, but feeding of 200 mg daily for the succeeding fourteen days produced milk that contained only 0.20 mg per liter. It is evidently more efficient to administer riboflavin directly to the foal than through the mare's milk, but the young foal's requirements for riboflavin are not generally known.

I am indebted to Mr Richard Nelson for his co-operation in caring for the mares, administering the riboflavin and collecting the samples of milk

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MEDICAL PROGRESS

GOLD THERAPY IN RHEUMATOID ARTHRITIS*

CHARLES L SHORT, M D,† WILLIAM W BECKMAN, M D,‡ AND WALTER BAUER, M D§

BOSTON

THE ease of evaluation of a therapeutic agent varies in proportion to the natural course of the disease for which it is to be used. In subacute bacterial endocarditis, which, if untreated, carries a nearly uniformly fatal prognosis, therapeutic success is evidenced by an appreciable increase in the survival rate. In lobar pneumonia, the specificity of the sulfonamides and penicillin has been established by a significant reduction in the mortality rate and rapid alterations in the clinical manifestations. The appraisal of therapy, however, in a benign, self-limited disease such as the common cold has been extremely difficult even in well controlled investigations. The last and most puzzling group to evaluate comprises chronic diseases of widely varying course and prone to spontaneous, unpredictable remissions and exacerbations. Examples of this group include bronchial asthma, peptic ulcer and rheumatoid arthritis. Neverthe-

less, from time to time, new methods of treating rheumatoid arthritis are claimed to have, if not specificity, at least a definite effect on the course of the disease. The early enthusiasm for each procedure is sooner or later dampened by the publication of critical, well controlled studies with essentially negative results.¹⁻³ An exception is gold therapy, introduced nearly twenty years ago, although its acclaimed specificity has occasionally been challenged in recent years.

The purpose of this report is not to present an inclusive review of the subject, which has been adequately performed elsewhere,⁴⁻¹¹ but to attempt to determine from the available evidence whether gold salts should be regarded as specific, as fulfilling an intermediate, adjuvant function or as having no established value. The harmful potentialities of gold treatment, including its toxicity, and the danger that, by dependence on gold alone, constitutional treatment and indicated orthopedic measures may be neglected must be carefully weighed.

HISTORICAL DEVELOPMENT

Although gold has been found effective in certain experimental infections,¹² its clinical use in modern

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times has been largely confined to patients with tuberculosis, lupus erythematosus of the discoid type and rheumatoid arthritis. Landé¹² and Pick¹⁴ in 1927 were the first to report on gold therapy in rheumatoid arthritis, but Forestier¹⁵⁻¹⁸ was responsible for its popularization in France and other European countries, England and finally the United States. His employment of gold in rheumatoid arthritis was founded on two now generally discredited premises that gold salts are effective in tuberculosis and that rheumatoid arthritis may be of tuberculous origin. The first British publication, by Slot and his co-workers¹⁹ in 1934, was followed by two American reports²⁰⁻²¹ in 1936. Since then, more than forty articles on chrysotherapy in rheumatoid arthritis have appeared in English, with conspicuously few adverse reports or opinions.^{20, 22-27}

MECHANISM OF ACTION

It may be stated at the outset that the mechanism of action of gold in rheumatoid arthritis is unknown and that the explanations offered rest entirely on hypothesis. Hartung²⁸ reported that the serums of patients receiving gold show a marked increase in bacteriostatic power against a strain of hemolytic streptococcus. This finding does not furnish an explanation of the mode of action of gold, since the etiology of rheumatoid arthritis, whether or not infectious, remains unknown. Others postulate a stimulation of the defense mechanisms of the body, presumably by deposition of gold in reticuloendothelial cells.²⁹ No evidence has been presented that gold has an analgesic effect or decreases joint swelling through diuresis, either of which might explain some of its favorable action. In view of the remissions in rheumatoid arthritis associated with intercurrent hepatic jaundice,³⁰ it has been suggested that the effect of gold is mediated by the production of liver damage, but demonstrable toxic effects on this organ have been rare, except in one series.⁴ Bayles and Riddell,³¹ in an attempt to find a common denominator for remissions associated with jaundice, pregnancy and gold, could demonstrate no increase in plasma lipids in gold-treated patients with rheumatoid arthritis. Finally, an impression has been gained from the literature^{32, 33} that patients exhibiting toxicity have nevertheless fared especially well so far as their arthritis was concerned. Such observations have led to the theory that the action of gold may depend on mild "protein shock," similar to the temporary ameliorating effect of intravenous typhoid vaccine.

PHARMACOLOGY

Knowledge of the clinical pharmacology of gold is largely derived from the extensive investigations of Freyberg and his co-workers,³⁴⁻³⁵ whose reports are freely utilized in this section. Although over twenty gold compounds have been used therapeutically,⁶⁻³⁶ only the preparations most frequently employed in recent years are discussed. All of them contain sulfur, but the gold content is believed to determine their therapeutic activity. Gold sodium thiosulfate (Allochrysine, Crisalbine and Sanocrysin) and gold sodium thiomalate (Myochrysine) are water-soluble salts. The former contains 37 per cent of gold and may be administered intravenously or intramuscularly, whereas the latter contains 50 per cent and is given intramuscularly. Both are absorbed with uniform rapidity and are regularly although slowly excreted. Gold thioglucose (Solganol B), although soluble in water, is administered in oil. This accounts for its slower and often variable absorption and the lower gold plasma levels observed, as compared with those seen in patients receiving other compounds of similar gold content (50 per cent). The same observation is true to an even greater extent of calcium thiomalate, which is insoluble in water, dispensed in oil suspension and also contains 50 per cent gold. Both salts, although apparently less toxic in the early stages of treatment owing to faulty absorption, may give rise to late toxicity, which is liable to be persistent and severe because of a relatively greater retention of gold associated with slow and irregular excretion.

Animal experiments suggest that the low plasma levels attained clinically with colloidal gold sulfide (Aurol-sulfide, containing 87 per cent of gold) are due to rapid disappearance of gold from the blood stream associated with phagocytization in reticuloendothelial cells, especially those of the liver and spleen.³⁵ Toxicity is thereby prevented, but opportunity for therapeutic action is minimized. In choosing a preparation for therapeutic use, the physician can logically adopt the conclusion that a water-soluble preparation should more readily reach the site of its action and, in addition, furnish warning of impending toxicity before the administration of an excessive amount.

Following absorption, gold is carried in an undetermined form in the protein fraction of the plasma. Its excretion is largely through the urine, although some appears in the stools. In spite of increasing accumulation in the body with repeated equal doses, plasma concentration remains relatively constant and excretion is increased only on the day of injection. Although the actual site of retention in the human body is not known, it is of practical importance that 70 to 80 per cent of the gold administered in a given period may be retained. Excretion may continue for months after the last injection, and may endure roughly in proportion to the amount given and to the rapidity of administration. Opportunity is thus presented for delayed and prolonged toxic manifestations. Snyder³⁷ cites a patient who developed a dermatitis that began one month after the last injection and persisted for nine months, she was still excreting gold five hun-

dred and ten days after treatment had been concluded

It was mentioned above that water-soluble compounds are preferable for therapeutic use. In view of their rapid absorption, no advantage is gained by intravenous injections, which may cause a sudden — possibly toxic — increase in concentration in the kidneys. The most effective and safest scheme of dosage remains to be determined. The trend in recent years has been to decrease the maximum weekly dose from 50 mg of metallic gold to 25³⁸⁻⁴⁰ or even 12.5 mg.⁴¹ It is believed that a smaller amount of gold in the body at any one time reduces the incidence, severity and duration of toxic manifestations.³⁵ Irrespective of the weekly dosage, a total of 500 mg of metallic gold usually comprises one course, the interval between courses varying from one to three months. The practitioner is confronted with a dilemma at this point. He must weigh the possibility of delayed toxicity against the possibility that the disease will relapse with discontinuance of therapy. To overcome this difficulty, it has been suggested that small maintenance doses between courses be used^{36, 41, 42} or that the drug be given continuously in small amounts for a prolonged period.⁴¹

Toxicity

The toxicity of gold compounds is fully described in a number of papers,^{4, 43, 44} including Sundelin's⁶ exhaustive monograph. The reported rates of toxicity range from 17 to 77 per cent, an average of 1 patient in 4 suffering some untoward effect. These reactions may involve almost every organ of the body, but the skin and mucous membranes (usually that of the mouth) are by far the most susceptible. Serious reactions include exfoliative dermatitis, hepatitis, colitis, purpura, agranulocytosis, encephalitis³⁷ and peripheral neuritis. An estimate made from a combined series of 1800 cases showed that 1 patient in 30 had a severe reaction and that 1 in 200 died as a result of gold therapy.³⁵

In one series, a reduction in incidence and severity of toxic reactions was ascribed to the use of smaller dosages³⁶; in another group similarly treated, however, there were 3 cases of exfoliative dermatitis and 2 of encephalitis among 100 patients.³⁸ There may be merit in beginning a course of therapy with small, gradually increasing amounts of gold so that sensitivity may be detected earlier and the reaction may be less severe and not so prolonged because of the presence of less gold in the body. Unfortunately, toxic manifestations may appear at the end of a course, may be delayed until the second or third course, or may even show up many months after the last injection. Toxicity is not related to the plasma level of gold, so that chemical control of administration cannot be employed.³⁵

Owing to the unpredictability of reactions, it is believed that, with the exception of renal damage,

they occur as an expression of sensitivity, either already present³⁷ or acquired during the administration of gold. Patch or intradermal tests are not helpful in determining which patients may be sensitive.^{35, 45} Careful clinical and laboratory examinations prior to the institution of treatment and before each dose, with special attention to the kidneys, liver, blood-forming organs and skin, are the only available safeguards. Urticaria, eczema and colitis furnish additional contraindications to the use of gold.

Treatment of the reaction, once started, has not been successful, although sodium thiosulfate, vitamins C and D, a high-calcium diet and shifting the acid-base equilibrium in either direction have been used.³⁵ A trial of BAL (British Anti-Lewisite), which has proved effective in arsenic intoxication,⁴⁶ is indicated. In spite of all precautions, the administration of gold carries a constant risk of a disabling toxic reaction. This fact must be kept in mind in any discussion of therapeutic results.

SELECTION OF PATIENTS

It is generally agreed that the effectiveness of gold in arthritis is limited to the rheumatoid type. There is no indication for its use in degenerative joint disease, gouty arthritis or arthritis associated with specific infections. Whether or not ankylosing spondylitis is regarded as a variety of rheumatoid arthritis, its treatment with gold has, except for one report,¹⁸ proved disappointing and therefore is usually not advised. Neither the age of the patient nor the duration of the disease is a factor in the selection of cases for treatment. Active arthritis should of course be present, but Forestier¹⁸ states that symptomatic relief may be obtained in apparently burnt-out cases with marked deformity. Early cases usually respond more favorably than those of longer duration, but on this point there is also some disagreement.^{5, 47} As pointed out below, patients in the early months of their first attack of rheumatoid arthritis are likelier to have spontaneous remissions irrespective of the treatment employed.⁴⁸ Therefore, a physician should not be criticized for delaying the use of a potentially dangerous drug at this stage of the disease.

RESULTS OF TREATMENT

Thirty-five papers in the English language on the results of gold therapy in rheumatoid arthritis have been reviewed. It is not possible to present the combined figures owing to the varying criteria utilized in judging improvement and the failure of some authors to state the degree of benefit obtained. An idea of the general trend may be gained, however, from the following percentages: gross improvement, of any degree — 84.0 per cent of 1943 patients, noteworthy objective improvement (usually a combination of the arrested and markedly improved group) — 59.3 per cent of 2924 patients,

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The rates of improvement cited in the preceding paragraph are impressive, but several criticisms and queries are immediately suggested. The first concerns the selection of patients. Had they been observed sufficiently long prior to chrysotherapy to make a coincidental remission unlikely? Were the patients hospitalized or receiving other treatment? The second criticism pertains to the course of untreated rheumatoid arthritis when it is untreated or when only general measures are used. Was a control group utilized, or were control series available in the literature for comparison? Finally, was the improvement held so that the use of the word "arrest" rather than "remission" was justified, or did a large proportion of patients rapidly revert to their former state? In six reports, the patients selected were considered "refractory" and received no other treatment than gold.^{26 40 45 51 52} When the available figures from these reports are combined, 41.6 per cent of the patients showed marked objective improvement, and 8.3 per cent entered on a remission. These percentages are definitely less striking than those for the combined series (59.3 and 22.6 per cent respectively) and suggest that spontaneous remissions are a factor in the more favorable results given for unselected series.

In two series the authors used comparable control groups. Ellman, Lawrence and Thorold⁵³ gave to one group of 30 patients two courses of gold, with an average weekly dose of 200 mg of Solganol B, to another, an average weekly dose of 100 mg, and to a third, a control group, injections of sterile oil. Although 76 per cent of the last group showed some improvement, compared to a total of 94 per cent in the two treated groups, in 37 per cent of the patients who received gold the disease became asymptomatic and the sedimentation rate returned to normal. These last results were realized in only 1 control patient. Objective improvement was also recorded more frequently in the treated patients, but the differences were not so striking. Those subjects receiving the larger dosage of gold showed a greater degree of improvement, but there was a corresponding rise in toxicity, with 1 death from agranulocytosis. Fraser⁵⁰ also divided his patients into two groups of about 50 each, one receiving an average weekly dosage of 100 mg of Myochrysine and the other an ampule containing the same constituents but without gold. Until the final observations were recorded at the end of a year, neither the author nor the patients knew which preparation had been

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tained of the likelihood of remission in early cases. Of 51 patients first seen within six months of the onset of their disease, 25 (49 per cent) were found to be in remission.

The tendency of a patient with rheumatoid arthritis who has shown improvement after one course of gold to relapse has been stressed since the original reports of Forestier.¹⁶⁻¹⁸ Certain authors found that further treatment again brings about improvement in the majority of cases, with a net

TABLE 1 *Results of General and Orthopedic Treatment in Rheumatoid Arthritis*

STATUS OF DISEASE	NO OF CASES	PERCENTAGE
Improved	145	52.9
In remission	45	16.4
Moderately improved	33	12.0
Slightly improved	67	24.5
Stationary	79	28.8
Worse	50	18.3
Total	274	

relapse rate of about 20 per cent,^{4, 8, 19} but Freyberg³⁵ states that retreatment has proved less satisfactory. The most recent study of relapses following gold therapy was presented at the 1946 meeting of the American Rheumatism Association by Ragan and Tyson,⁴² who reported on follow-up studies for at least three years of 142 patients, 50 per cent of whom had shown objective improvement following one or more courses of gold. Only 13 per cent had maintained their improvement for periods ranging from forty-five to seventy-eight months, and a five-year cure was obtained in only 9 cases. About

had been progressive or in a steady state for at least six months. Otherwise, they were unselected and represented a cross-section of the disease. There were 15 males and 32 females in the series, with ages ranging from eleven to sixty-eight years. The duration of the disease was under five years in about half the patients, but two years or under in only 5 and less than one year in none. The total severity of the disease was classified as follows: mild, 7; moderate, 31; and marked, 9. Most patients received Myochrysine, with a maximum weekly dosage of 100 mg. An attempt was made to give each patient at least two courses, each totaling 1 gm of the drug. In 12, the treatment had to be stopped on account of toxicity before a full course had been given. The remaining 35 received a total of sixty-seven courses. Only a few of the patients receiving gold were hospitalized during treatment, but many of the others continued with extra rest, analgesics, a good diet and exercises, although general treatment was not stressed during this period.

The results of therapy are shown in Table 2, along with the rate of relapse following treatment, on the basis of the most recent follow-up study of patients showing improvement. In each case, any improvement recorded was objective and definite, so that the results may be compared with the control series in Table 1. Some improvement was observed in nearly the same proportion of patients treated with gold as in the controls, but none of the gold-treated patients entered on a remission. This difference might be expected from the fact that the patients receiving gold were selected for resistance to ordinary forms of treatment. From a

TABLE 2 *Results of Gold Therapy in Rheumatoid Arthritis*

STATUS OF DISEASE	NO OF CASES	PER CENTAGE	NO OF RELAPSES	NET IMPROVEMENT	
				NO OF CASES	PER CENTAGE
Improved	21	60	13	8	23
In remission	0	0	0	0	0
Moderately improved	7	20	6	1	3
Slightly improved	14	40	7	7	20
Stationary or worse	14				
Total	35				

75 per cent of patients who had experienced objective improvement had relapsed, although usually not to a condition as severe as their original disease. As mentioned above these authors hope to lessen the rate of relapse by small maintenance doses at intervals of several weeks. From these figures, the conclusion is inescapable that gold therapy, as usually administered, exerts at best a transitory effect on the course of rheumatoid arthritis.

Experience at the Massachusetts General Hospital with gold therapy in rheumatoid arthritis is limited to 47 patients, in all of whom the disease

study of the two tables, it is difficult to find evidence that gold therapy exerted any noteworthy effect on the course of the disease.

Sedimentation rates were determined at regular intervals in all cases. The results roughly paralleled the degree of clinical improvement, with normal values reached in all but 1 of the moderately improved patients, but an appreciable fall took place in only half of those showing slight improvement. The incidence of toxicity was high. In addition to the 12 in whom treatment had to be stopped during the first course, in 5 the dosage was inter-

rupted during the second or third course, and another 5 suffered from delayed manifestations of toxicity, sometimes months after the course had been finished. One patient developed a mild purpuric eruption after 0.9 gm of Myochrysine, when treatment was stopped, over four months after the last injection, purpura reappeared in a generalized form, with bleeding from the gums and nose. Platelets were found to be absent from the blood smear. In spite of repeated transfusions, the patient continued to show evidence of widespread bleeding, and death took place in five weeks. At autopsy bilateral subdural hematomas were found to be the principal cause of death.

CONCLUSIONS

The first question that this report attempted to answer is whether gold therapy may be regarded as a specific and constantly effective treatment for rheumatoid arthritis. That the activity of the disease process is reversible is shown both by spontaneous remissions and by those encountered in pregnancy and intercurrent jaundice. From the small percentage of patients in the literature in whom the disease was arrested subsequent to gold treatment and from our own experience, the answer seems evident that gold cannot rightfully be included in the select group of specific agents available in medical therapy, such as the sulfonamides and penicillin in bacterial infections and the arsenicals and heavy metals in syphilis. Corroboration of this conclusion is furnished by the statements of a number of others who have had experience with gold therapy and who believe that this method should supplement general measures or constitute only a part of a broad therapeutic program.³⁵⁻⁵³

It is more difficult to furnish a categorical answer to the question whether gold is of some benefit to the patient with rheumatoid arthritis and whether its use is therefore justified in a patient failing to respond to conservative measures. Two control studies apparently demonstrate an additive therapeutic effect on the part of gold during relatively brief periods of observation.⁵⁰⁻⁵³ Otherwise, the results obtained with gold may be approximated with those in patients given general, conservative treatment. A careful follow-up study of patients improving during gold therapy reveals a high percentage of relapses, so that the net gain is slight. There is even an indication that the natural, fluctuant course of the disease is largely responsible for the results reported in such cases. The burden of proof is still on the proponents of gold therapy to demonstrate by adequately controlled studies with a follow-up of three to five years that a significant effect is exerted on the course of rheumatoid arthritis by the administration of gold salts.

Finally, the unpredictable, unpreventable and at times irremediable toxic manifestations of gold therapy cannot be overlooked. If the specificity

of gold were established, this risk would be justifiable in a disease that bears the implications of lasting invalidism. With the case as yet unproved for its place as a palliative or adjuvant remedy in rheumatoid arthritis, the hazard of this form of therapy should furnish the decisive argument against its general use.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Annual Meeting, May 21, 1946

THE annual meeting of the Council was called to order by the president, Dr Reginald Fitz, Suffolk, on Tuesday, May 21, 1946, at 7 00 p m, in the Georgian Room of the Hotel Statler, Boston, 191 councilors (Appendix No 1) were present

In opening the meeting the President read the following obituary

The President regrets to report the death of John Joseph Elliott, a councilor from the Norfolk District He was in his fiftieth year

Dr Elliott received his degree from the Hahnemann Medical College in 1921 in Pottsville, Pennsylvania, where he spent his early days, he attained high distinction as an athlete, excelling in football, basketball, baseball and track When he received his medical diploma he came to Boston and here he remained, after serving an internship and residency at the Massachusetts Memorial Hospitals In 1923 he was appointed to the staff of that institution and was promoted in the course of twelve years from the rank of second assistant obstetrician to that of obstetrician

Perhaps his flair for athletics enabled him to understand how the minds of young men react In any event, he soon demonstrated outstanding ability as a teacher, became assistant in the Department of Obstetrics at Boston University in 1926, and was advanced through the grades of instructor and assistant professor until finally, in 1944, he was created associate professor

He was a successful, hard-working physician, but in addition to leading a busy life as practitioner and teacher, he found time in which to cultivate hobbies in the field of sport He was a recognized authority on the technical phases of basketball, track and baseball, he was consulting physician to the Boston College football team, he stimulated interest, locally, in pigeon racing, and he achieved national fame as horseman and owner of champion ponies

He became a fellow of the Massachusetts Medical Society in 1926, serving on the Council during 1940, 1941 and 1942, and from 1945 until his death He despised unfairness in any form, his judgment always was sound and unbiased, and thus he was a valuable member

Besides being a fellow of the Massachusetts Medical Society and the American Medical Association, he belonged to the American College of Surgeons, the New England Obstetrical and Gynecological Association and the West Roxbury Medical Club

Dr Elliott is survived by his widow, two sons and a daughter

The President asked the councilors to stand for one minute in silent tribute to the memory of Dr Elliott

In accordance with the vote of the Council in February, 1946, the President announced the following appointments

Committee to Assist the Council on Medical Education and Hospitals of the American Medical Association in the Provisional Approval of Certain Massachusetts Hospitals

Robert T Monroe, Norfolk, chairman
H Quimby Gallupe, Middlesex South
Walter G Phippen, Essex South
Michael A Tighe, Middlesex North
Charles F Wilinsky, Suffolk

Committee to Review the Matter of Malpractice Insurance

Carl Bearse, Norfolk, chairman
William J Brickley, Suffolk
Edwin D Gardner, Bristol South
Daniel B Reardon, Norfolk South
Guy L Richardson, Essex North

Committee on Postgraduate Assembly

Leroy E Parkins, Suffolk, chairman
Harold G Giddings, Middlesex South
Frederick S Hopkins, Hampden
Charles J Kickham, Norfolk
Robert N Nye, Suffolk

The President asked for confirmation of these appointments It was so ordered by vote of the Council

The Secretary submitted the record of the meeting of the Council held on February 6, 1946, as published in the May 2, 1946, issue of *The New England Journal of Medicine*, and moved its adoption This motion was seconded, and it was so ordered by vote of the Council

REPORT OF THE TREASURER

This report (Appendix No 2) was offered by Dr Eliot Hubbard, Jr, as published in the pamphlet of

advance information. He moved its adoption. This motion was seconded and it was so ordered by vote of the Council.

REPORTS OF COMMITTEES

Executive Committee — Dr. Michael A. Tighe, Middlesex North, secretary.

The Secretary submitted the report (Appendix No. 3) as published in the circular of advance information and moved its acceptance. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Auditing Committee — Dr. William B. Robbins, Suffolk, chairman, and Dr. Arthur W. Carr, Plymouth.

This report, which was offered by the chairman, is as follows:

The Auditing Committee appointed the firm of Hartshorn and Walter, accountants and auditors to audit the books and accounts of the Massachusetts Medical Society. This audit and account are hereby approved by us.

The analysis of the revenues and expenses of the Society, and the balance sheet of the condition of the funds of the Society, have been inspected and approved by us.

Dr. Robbins moved the adoption of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Arrangements — Dr. Roy J. Heffernan, Norfolk, chairman.

This report, which is as follows, was offered by the chairman:

The program of the annual meeting is our final report. You will be pleased to note that, in addition to the usual scientific program, the committee has revived some of the pleasant antebellum features, namely, the activities for the distaff side and the annual golf tournament.

It should be emphasized that the commercial exhibits supply the wherewithal for our annual meeting. All members are urged to visit these exhibits frequently.

I wish to thank the other members of the Committee on Arrangements for their loyal and efficient co-operation. Our chief worry during the past year was that something might happen to Mr. Robert Boyd before our plans were consummated. I cannot imagine how the committee could function without his gracious assistance. We are very grateful to him.

Dr. Heffernan, in offering the report, said that it contained one recommendation that the fellows be urged to visit the commercial exhibits several times during the annual meeting.

He moved the adoption of the report and the recommendation contained in it. This motion was seconded by a councilor.

The President called on the Secretary for such comment as the Executive Committee might wish to make regarding this report. The Secretary said that the Executive Committee approved of the recommendation contained in the report and, in the furtherance of its objective, recommended additionally that the *New England Journal of Medicine* carry suitable references to these exhibits and that the several chairmen who preside over the exercises of the annual meeting be instructed to call, at least

twice daily, the attention of the gathering to them and to the importance of paying them a visit.

These additional recommendations, having been accepted by the maker of the motion and its seconder, became part of the original motion. The motion was adopted by vote of the Council.

Committee on Medical Defense — Dr. Arthur W. Allen, Suffolk, chairman.

In the absence of the chairman the Secretary offered the report, which is as follows:

We now have five malpractice suits pending. No new cases developed during the past year. Six cases were disposed of during the year.

The total bills for legal services and disbursements for the year 1945 amounted to \$571.67.

The Secretary moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the committee.

Committee on Medical Education — Dr. Robert T. Monroe, Norfolk, chairman.

This report (Appendix No. 4), as it appeared in the circular of advance information, was submitted by the chairman. He added that it was purely informational. He moved adoption of the report. This motion was seconded by a councilor.

The President called on the Secretary for such comment as the Executive Committee might wish to make regarding the report. The Secretary reported for the Executive Committee, as follows:

This report is an excellent factual study of correlated material brought together from many sources. Its conclusions are soundly drawn. The Executive Committee is aware that the stimulus to the resolution offered by Dr. Morgan, by which the Council authorized this study, came about largely as the result of inquiry by members of the Massachusetts Legislature as to the need of additional medical schools in Massachusetts.

Because this report now makes such information readily available, the Executive Committee in addition to recommending that the report be accepted by the Council, further recommends that the Council specifically direct the attention of the Committee on Legislation to the report, for such use as this latter committee may deem wise. In so directing the attention of the Committee on Legislation to this report, the Executive Committee points out that Table 4, as it relates to the rejections listed, without further explanation, might be subject to serious misunderstanding. In this connection the Executive Committee would have the Council and the Committee on Legislation know that most candidates apply simultaneously to many medical schools, and that those rejected by one school frequently find places in another. The committee has it on competent authority that a little over 50 per cent of all applicants ultimately find places in some medical school.

The maker of the motion and the seconder having accepted the recommendation of the Executive Committee, it became a part of the original motion, which was adopted by vote of the Council.

Committee on Publications — Dr. Richard M. Smith, Suffolk, chairman.

This report (Appendix No. 5) was submitted as published in the circular of advance information.

The chairman, in offering the report, called the Council's attention to the fact that we are now in the twenty-fifth year during which the *New England Journal of Medicine* has been operated by the Massachusetts Medical Society.

The report stated that Dr John B Youmans, formerly chief of the Nutrition Branch of the Office of the Surgeon General and associate professor of medicine at Nashville, Tennessee, had been selected to deliver the Shattuck Lecture during the annual meeting of the Society in 1946, that a directory of the fellows had been published during the year (1945) and that the accounts of the *Journal* had been audited and found to be in order.

The report, in calling attention to the excellent record of the *Journal* during the last year, spoke highly of the managing editor, Dr Robert N Nye, the assistant editor, Miss Davies, the associate editors and the members of the Editorial Board.

He quoted from the report of the managing editor to the effect that there was a substantial net increase in the circulation during the year 1945 and not only that the *Journal* had not used any of the monies appropriated by the Society for its use in 1945 but also that on December 31, 1945, it paid to the Treasurer of the Society the sum of \$22,800.00. The report said that the pagination of the *Journal* had been increased and that the stock used was heavier, all of which was made possible by the removal of governmental limitations on paper.

The report said that the difficulties in the matter of printing were still present, and that the increased circulation and the shifting of addresses brought about by the war present a major problem. If the *Journal* is to function properly, additional office space must be provided.

Dr Smith moved the adoption of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Public Health—Dr Roy J Ward, Worcester, chairman.

This report (Appendix No 6) was offered by the chairman as published in the circular of advance information. He pointed out that it contained a recommendation that the President be authorized to take the initiative in aiding the four district societies concerned in selecting suitable representation on the Greater Boston Nursing Council. He moved the adoption of the report and the recommendation contained in it. This motion was seconded.

The President called on the Secretary for such comment as the Executive Committee might wish to make regarding this report. The Secretary reported for the Executive Committee, as follows:

The Executive Committee notes that this report contains a recommendation to the effect that the president of the Society be authorized to take the initiative in aiding the four district societies concerned in selecting suitable representation on the Greater Boston Nursing Council. The Executive Committee disapproves of this recommendation.

It believes that because of the Society's statewide character it should not associate itself with an organization that is purely sectional in its scope and purposes. The Executive Committee recommends in this connection that the Council reaffirm its stand in this matter as taken on October 6, 1937.

The Executive Committee further recommends that the Council instruct the Secretary to write to Miss Tracy, of the Greater Boston Nursing Council, advising her of the Society's sympathetic interest in this matter and recommending that she make contact with the district societies concerned.

He moved, by way of amending the motion, the adoption of the recommendations of the Executive Committee. This motion was seconded.

Dr Elmer S Bagnall, Essex North, said that it was his impression that Miss Tracy had endeavored unsuccessfully to make contact with the district societies concerned. He expressed his belief that, in turning down the recommendation of the Committee on Public Health, the Council was sticking too closely to the proprieties of the situation. If Miss Tracy's request, he continued, were given serious thought by the district societies concerned, it would not be necessary for the Society to take action. Finally he expressed his opinion that the Society should not turn down a request to use its good offices in a matter that was of public interest.

Dr Alexander J A Campbell, Suffolk, said that he spoke under instruction from the Suffolk District Medical Society, whose opinion was unanimous that the Massachusetts Medical Society has the responsibility of co-operating with the Massachusetts Nursing Council in its program to develop the best possible form of nursing organization in Massachusetts and that the Society should take whatever appropriate action might be deemed necessary, because the Massachusetts Nursing Council as such is not active and because its work is largely being carried on by the Greater Boston Nursing Council.

He moved as an amendment to the amendment that the President appoint a committee to confer with the chairman of the Greater Boston Nursing Council for the purpose of determining ways and means by which the common interests of these closely allied professions might be better developed.

Dr Peirce H Leavitt, Plymouth, spoke for the adoption of the recommendations of the Executive Committee.

The President elected first to put the recommendation offered by the Committee on Public Health. This was lost by vote of the Council. The President then put the recommendations offered by the Executive Committee. These recommendations were adopted by vote of the Council.

This matter having thus been disposed of, the recommendation offered by the representative from Suffolk was not put to a vote.

Committee on Society Headquarters—Dr Frank R Ober, Suffolk, chairman.

This report, which was offered by the chairman, is as follows:

The Committee on Society Headquarters still continues to give serious study to the possible expansion of the Society Headquarters.

It has, however, nothing definite to report in the matter at this time.

The chairman moved the acceptance of this report. The motion was seconded, and it was so ordered by vote of the Council.

Committee on Physical Medicine — Dr Arthur L Watkins, Middlesex South, chairman

This report, which is as follows, was submitted by the chairman:

As no new or special problems have been laid before this committee, its report is purely to inform the Society on developments in the field of physical medicine thought to be of interest. An outstanding event has been a more generally accepted recognition of the needs for expansion of knowledge in physical medicine and of more widespread utilization of measures already known to be effective in aiding recovery from disease and injury and occasionally in prevention and diagnosis. The gift of Bernard M. Baruch to foster research and teaching is noteworthy. At the Harvard Medical School a fellowship program was inaugurated one year ago to train promising men to become investigators and teachers. These fellowships extend over a three-year period including time for fundamental research. A three months' course which is offered at the Massachusetts Institute of Technology in biophysics aimed to instruct physicians in methods of instrumentation applicable to medical problems is another valuable Baruch project. It is expected that physical medicine will play an increasingly important role, particularly in problems of rehabilitation. All physicians are accordingly urged to acquaint themselves with the therapeutic possibilities of physical and occupational therapy. An annual progress report on research in physical medicine has been prepared for publication in the *New England Journal of Medicine* in order that the general practitioner may become familiar with the scientific background of physical medicine today.

The chairman moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Public Relations — Dr Albert A Hornor, Suffolk, secretary

This report, which is as follows, was submitted by Dr Hornor:

The Secretary of the Committee on Public Relations has notified the secretaries of the district medical societies of the approval of the committee of the action taken by a group of physicians in Lowell, independent of the Massachusetts Medical Society, to educate their local public through advertising. Included in the letter were examples of the advertisements that had been put out in Lowell and in Newton and other groups. No action on this matter is requested.

The Committee on Public Relations has reviewed the report of the Special Committee Appointed to Confer with General Hawley anent the medical care of veterans in private hospitals and in the veterans' homes. The committee has likewise reviewed a schedule of fees intended to cover the charges for such medical care. The committee approved the report and the fee schedule.

The Committee on Public Relations approved the project of enrolling members of the Massachusetts Medical Society in the Blue Cross and recommends to the Council that this be effected in the manner considered most efficient by the secretary of the Massachusetts Medical Society and by the officials of Blue Cross.

The Committee on Public Relations is unwilling to take a stand on the question as to enrollment of the members of the Society in the Blue Shield. The question which is involved here is whether or not enrollment of members in

the Blue Shield might or might not affect the tradition whereby one doctor supplied medical care to another or to the other's family, without charge. The Committee on Public Relations has requested that Dr Milton Quinn, chairman of the subcommittee that has investigated this question, present the problem to the Council.

In discussing this report, Dr Hornor said it contained a recommendation that the Council approve of the enrollment of the members of the Massachusetts Medical Society in the Blue Cross in such a manner as is considered most efficient by the secretary of the Society and the officials of the Blue Cross. He moved the adoption of this recommendation. The motion was seconded, and it was so ordered by vote of the Council.

Dr Hornor then stated that the matter of enrolling the members of the Society in the Blue Shield had been discussed by the committee, which offered no recommendation in this regard.

He called on Dr Milton J Quinn, Middlesex East, to present the argument for such enrollment. Dr. Quinn spoke as follows:

The members of the Committee on Public Relations declined to take definite action in the problem of the enrollment in the Blue Shield on the ground that it involved a very important principle in the practice of medicine, namely, the question of cash payment from one physician to another for services rendered.

Gratuitous care by one physician to another and his family has been a sacred principle of our profession throughout the centuries. It will continue thus in many quarters well into the foreseeable future. There are good reasons why strict adherence to this worthy principle has not always been practiced. A sort of a barter plan grew in popularity. A pair of tonsils is swapped for a beautiful Gladstone bag. A broken leg for a savings bond, which is approaching more closely a cash exchange and so on.

Some physicians and their families are so insured that in the event of accident or illness the attending physician is requested to send a bill for his services so that the insured may receive certain allowances. With communication and transport as they are today, it means overburdening more people in our profession with the care of doctors and their families. Some of the load is carried by all.

The interested committees of this Council have recently had under consideration a fee schedule applicable to war veterans and their dependents. This will include, I am sure, some doctors and their families. Shall we accept such fees? Shall we accept the fees offered by the Blue Shield? The problem now presented to the Council is whether or not it will approve the enrollment of the members of the Massachusetts Medical Society in the Blue Shield in a manner as suggested in the Blue Cross enrollment mentioned by Dr Hornor.

At this point in the meeting, the President declared a short recess so as to afford those in the rear of the room to come forward, where ample seating space was available.

When the Council reconvened, the President asked the Secretary to state the views of the Executive Committee on this subject. The Secretary spoke as follows:

In the discussion attending this subject before the Executive Committee, Dr Milton Quinn was heard. He expressed it as his belief that many members of the Society were overburdened by the care of other physicians and their families. He saw no reason why individual members of the Society might not join the Blue Shield, if they so desired. The question at issue, as he defined it, was whether or not the Massachusetts Medical Society should endorse their joining.

In connection with that subject, Section 2, Article II, of the "Principles of Medical Ethics" of the American Medical Association was read into the record. This section reads as follows:

When a physician from a distance is called on to advise another physician or one of his family dependents, and the physician to whom the service is rendered is in easy financial circumstances, a compensation that will at least meet the traveling expenses of the visiting physician should be proffered. When such a service requires an absence from the accustomed field of professional work of the visitor that might reasonably be expected to entail a pecuniary loss, such loss should, in part at least, be provided for in the compensation offered.

It was pointed out that at least inferentially, except under the circumstances outlined, this section indicates that it is not considered good medical ethics for one physician to charge another for services rendered.

The Executive Committee likewise offers no recommendation regarding this matter.

The President stated that two committees had studied this matter and had apparently arrived at no conclusion.

Dr. Ralph R. Stratton, Middlesex East, chairman of the Committee on Ethics and Discipline, was recognized by the chair. Dr. Stratton spoke as follows:

My feeling is strong that the article of the ethics of the American Medical Association in regard to this matter should stand. I believe that any man who is asked by a neighboring or fellow physician to take care of his family should feel complimented and be glad to attend that family for nothing, except that his expenses might be paid if the person receiving the service is in easy circumstances. I am heartily opposed to joining the Blue Shield in order that we might be paid for taking care of our own in their need.

Dr. Stratton's remarks were greeted with applause.

Dr. Charles J. E. Kickham, Norfolk, moved that the subject under discussion be laid on the table. This motion was seconded, and it was so ordered by vote of the Council.

Dr. Hornor moved that the report of the Committee on Public Relations, as a whole, excluding the part referring to enrollment in the Blue Shield, be adopted. This motion was seconded, and it was so ordered by vote of the Council.

By permission of the President, Dr. Daniel J. Ellison, Middlesex North, chairman of the Subcommittee Appointed to Confer with the Massachusetts Industrial Accident Board, offered the following supplement to the report of the Committee on Public Relations:

Some months ago the Norfolk District Medical Society brought in a resolution which called for a review of the fees allowed by the Massachusetts Industrial Accident Board. The matter was referred to the subcommittee, consisting of Dr. David D. Scannell, Dr. Gordon M. Morrison and myself. The work of this subcommittee in this respect was finished yesterday morning.

Henceforth a physician examining a workman who has developed a hernia as the result of his occupation is allowed a fee of \$3.00 for an examination looking toward the establishment of this as a fact, when such a physician does not perform an operation. The surgeon operating on such an individual is allowed a fee of \$75.00 for single and \$100.00 for a double hernia. The operating surgeon is allowed no examination fee.

House calls to individuals injured in industry will be allowed at the rate of \$4.00 per call. Hospital calls under these same circumstances will be at the rate of \$3.00 per call. Office calls will be at the rate of \$2.50 per call.

These represent substantial increases in the fees allowed for the medical care of industrial accident cases.

We are very appreciative of the efforts of those groups concerned with these successful negotiations. Notable among those groups were the Massachusetts Industrial Accident Board, Mrs. Emma S. Tousant, chairman, the Medical Advisory Committee of the Industrial Accident Board, Dr. Cadis Phipps, chairman, and the subcommittee of the Committee on Public Relations.

Dr. Ellison moved the acceptance of the supplementary report. This motion was seconded, and it was so ordered by vote of the Council. (Dr. Ellison left the platform amid applause.)

Committee on Postwar Planning — Dr. Howard F. Root, Suffolk, chairman.

Dr. Root submitted the report (Appendix No. 7) as published in the circular of advance information.

It was stated that the Commonwealth, for purposes of postgraduate education, had been divided into seven districts, all of which had at least two sets of courses except District No. 1, in which courses were at the moment in preparation. In District No. 7, which includes the Greater Boston area, bi-weekly postgraduate programs were held from February 18 to May 15, 1946. Over a thousand physicians were registered for these courses. The average attendance at each exercise was over 500.

The report said that the Subcommittee on Veterans Affairs had been set up and a questionnaire distributed at the bi-weekly exercises mentioned above. The replies to this questionnaire indicated the need of office space, telephone listing and the enlargement of the activities of the Information Bureau at 8 Fenway.

The report decried the failure of the district societies to fill out completely the questionnaire sent out by the American Medical Association. This failure made it impossible for the Information Bureau to give advice regarding opportunities for practice in various parts of the Commonwealth.

Finally, the report mentioned a conference that was held with the Massachusetts Hospital Association concerning the provision of hospital appointments for veterans.

Supplementing the report, Dr. Root said that during the period of the annual meeting a questionnaire would be found at the registration desk, the purpose of which was to obtain information from the physicians in attendance, veterans and otherwise, regarding how the Committee on Postwar Planning might better serve the interests of the returning veteran doctor.

He moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Legislation — Dr. David L. Belding, Norfolk South, chairman.

Dr. Belding submitted the report (Appendix No. 8) as published in the pamphlet of advance information. The report was debated in executive session.

Dr Belding moved the adoption of the report and their recommendations contained in it. This motion was seconded.

The President called on the Secretary for such comment as the Executive Committee wished to make regarding this report. The Secretary stated that the Executive Committee, in approving of the report and the recommendations contained in it, applauded the wisdom that it displayed.

The motion was passed by vote of the Council (Dr Belding left the platform amid loud and prolonged applause).

Massachusetts Delegates to the Council of the New England State Medical Societies

This report (Appendix No 9) was offered by the Secretary as it appeared in the pamphlet of advance information. He moved its acceptance. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary said that the Executive Committee recommended, subject to the approval of the Committee on Finance, that the Council appropriate the sum of \$100.00 for the use of the New England Council during the ensuing year. In reference to this recommendation he stated that each medical society in the Council would appropriate a like amount. He moved the adoption of the recommendation. The motion was seconded, and it was so ordered by vote of the Council.

Committee on Postwar Loan Fund—Dr George Leonard Schadt, Hampden, chairman

This report, which is as follows, was offered by the chairman:

This report of the Committee on Postwar Loan Fund is informational only.

This fund was activated by the Council at its meeting in October, 1945, and since that date eleven loans have been made, each for five hundred dollars. In addition, there are three loans pending.

Forty-four requests for information concerning the loan have been received by the committee.

Dr Schadt moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Report of the Massachusetts Representative to the House of Delegates of the American Medical Association

This report (Appendix No 10), as published in the pamphlet of advance information, was submitted by Dr David D Scannell, Norfolk. He moved its acceptance. This motion was seconded, and it was so ordered by vote of the Council.

Committee Appointed to Make Recommendations for Directors of the Blue Shield—Dr Leland S McKittrick, Suffolk, chairman

In the absence of Dr McKittrick, the Secretary submitted the following report:

The Committee to Make Recommendations for Directors of the Blue Shield submits the names of the following men:

To hold office until 1947:

Mr Philip Morgan — reappointment
Dr Norman A Welch — reappointment
Dr Arthur W Allen — reappointment
Mr J H Humphreys — reappointment
Mr Roswell Phelps — reappointment

To hold office until 1948:

Dr Eugene Walker, superintendent Springfield Hospital, Springfield, to replace Mr Oliver G Pratt (resigned)
Mr Thomas G Brown — reappointment
Dr Elmer S Bagnall — reappointment
Mr Ernest A Johnson — reappointment
Mr Daniel J Boyle — reappointment

To hold office until 1949:

Mr Hugh Nawn, president, Hugh Nawn Incorporated Boston, to replace Mr Thomas Dignan (term expired)
Mr Joseph K Miliken, Jr, superintendent, Mr Hope Finishing Company, Dighton, to replace Mr P A O'Connell (term expired)
Dr Samuel A Robins — reappointment
Dr James C McCann — reappointment
Mr Harold B Leland — reappointment

The Secretary moved the acceptance of this report. This motion was seconded, and it was so ordered by vote of the Council.

Committee Appointed to Confer with the Massachusetts Hospital Association—Dr Walter G Phippen, Essex South, chairman

The report, which is as follows, was presented by the chairman:

This committee was instructed to consult with the Massachusetts Hospital Association as to activation of the Galluppe Plan to determine the position graduates of substandard schools might take on hospital staffs.

In accordance with this vote the chairman wrote to the president of the Massachusetts Hospital Association and received the following reply which is self-explanatory:

March 7 1946

Dr Walter G Phippen
31 Chestnut Street
Salem Massachusetts

Dear Doctor Phippen:

The recommendations of the Council of the Massachusetts Medical Society bearing on graduates of substandard schools, which you sent me recently, were presented to the trustees of the Massachusetts Hospital Association. On that same occasion Dr Galluppe sat in with the trustees giving his endorsement to the recommendations and outlined his plan for making these recommendations effective in the Waltham Hospital.

The trustees of the Massachusetts Hospital Association were entirely in sympathy with this movement to provide opportunities in hospitals for these graduates of substandard schools and agreed to co-operate in the movement.

The manner of doing so is to be something like this:

To inform the member hospitals of the Association by letter that the trustees of the Massachusetts Hospital Association believe it desirable that graduates of substandard schools be given opportunities in hospitals under suitable regulation.

To advise the member hospitals that we endorse the recommendations of the Massachusetts Medical Society looking to this end.

That we send each hospital of the Association a copy of these recommendations of the Council.

I believe that the secretary of the Association is to be furnished with a supply of these printed recommendations, a copy of which you sent me and which I left with the secretary. These are to be included in a letter which goes to the membership.

Having thus agreed with your committee and the Council of the Massachusetts Medical Society and moving in this way to give effect to the recommendations it seems to me it should about meet the needs of the present.

In connection with that subject, Section 2, Article II, of the "Principles of Medical Ethics" of the American Medical Association was read into the record. This section reads as follows:

When a physician from a distance is called on to advise another physician or one of his family dependents, and the physician to whom the service is rendered is in easy financial circumstances, a compensation that will at least meet the traveling expenses of the visiting physician should be proffered. When such a service requires an absence from the accustomed field of professional work of the visitor that might reasonably be expected to entail a pecuniary loss, such loss should, in part at least, be provided for in the compensation offered.

It was pointed out that at least inferentially, except under the circumstances outlined, this section indicates that it is not considered good medical ethics for one physician to charge another for services rendered.

The Executive Committee likewise offers no recommendation regarding this matter.

The President stated that two committees had studied this matter and had apparently arrived at no conclusion.

Dr. Ralph R. Stratton, Middlesex East, chairman of the Committee on Ethics and Discipline, was recognized by the chair. Dr. Stratton spoke as follows:

My feeling is strong that the article of the ethics of the American Medical Association in regard to this matter should stand. I believe that any man who is asked by a neighboring or fellow physician to take care of his family should feel complimented and be glad to attend that family for nothing, except that his expenses might be paid if the person receiving the service is in easy circumstances. I am heartily opposed to joining the Blue Shield in order that we might be paid for taking care of our own in their need.

Dr. Stratton's remarks were greeted with applause.

Dr. Charles J. E. Kickham, Norfolk, moved that the subject under discussion be laid on the table. This motion was seconded, and it was so ordered by vote of the Council.

Dr. Hornor moved that the report of the Committee on Public Relations, as a whole, excluding the part referring to enrollment in the Blue Shield, be adopted. This motion was seconded, and it was so ordered by vote of the Council.

By permission of the President, Dr. Daniel J. Ellison, Middlesex North, chairman of the Subcommittee Appointed to Confer with the Massachusetts Industrial Accident Board, offered the following supplement to the report of the Committee on Public Relations:

Some months ago the Norfolk District Medical Society brought in a resolution which called for a review of the fees allowed by the Massachusetts Industrial Accident Board. The matter was referred to the subcommittee, consisting of Dr. David D. Scannell, Dr. Gordon M. Morrison and myself. The work of this subcommittee in this respect was finished yesterday morning.

Henceforth a physician examining a workman who has developed a hernia as the result of his occupation is allowed a fee of \$3.00 for an examination looking toward the establishment of this as a fact, when such a physician does not perform an operation. The surgeon operating on such an individual is allowed a fee of \$75.00 for single and \$100.00 for a double hernia. The operating surgeon is allowed no examination fee.

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These represent substantial increases in the fees allowed for the medical care of industrial accident cases.

We are very appreciative of the efforts of those groups concerned with these successful negotiations. ^{Noted} among those groups were the Massachusetts Industrial Accident Board, Mrs. Emma S. Tousant, chairman, the Medical Advisory Committee of the Industrial Accident Board, Dr. Cadis Phipps, chairman, and the subcommittee of the Committee on Public Relations.

Dr. Ellison moved the acceptance of the supplementary report. This motion was seconded, and it was so ordered by vote of the Council. (Dr. Ellison left the platform amid applause.)

Committee on Postwar Planning — Dr. Howard F. Root, Suffolk, chairman.

Dr. Root submitted the report (Appendix No. 7) as published in the circular of advance information.

It was stated that the Commonwealth, for purposes of postgraduate education, had been divided into seven districts, all of which had at least two sets of courses except District No. 1, in which courses were at the moment in preparation. In District No. 7, which includes the Greater Boston area, bi-weekly postgraduate programs were held from February 18 to May 15, 1946. Over a thousand physicians were registered for these courses. The average attendance at each exercise was over 500.

The report said that the Subcommittee on Veterans Affairs had been set up and a questionnaire distributed at the bi-weekly exercises mentioned above. The replies to this questionnaire indicated the need of office space, telephone listing and the enlargement of the activities of the Information Bureau at 8 Fenway.

The report decried the failure of the district societies to fill out completely the questionnaire sent out by the American Medical Association. This failure made it impossible for the Information Bureau to give advice regarding opportunities for practice in various parts of the Commonwealth.

Finally, the report mentioned a conference that was held with the Massachusetts Hospital Association concerning the provision of hospital appointments for veterans.

Supplementing the report, Dr. Root said that during the period of the annual meeting a questionnaire would be found at the registration desk, the purpose of which was to obtain information from the physicians in attendance, veterans and otherwise, regarding how the Committee on Postwar Planning might better serve the interests of the returning veteran doctor.

He moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Committee on Legislation — Dr. David L. Belding, Norfolk South, chairman.

Dr. Belding submitted the report (Appendix No. 8) as published in the pamphlet of advance information. The report was debated in executive session.

talked very plainly. We told them that it was a matter of education, that we believed that they were not so well educated as they might have been, and they admitted it. I have never found one yet that did not regret that he had gone to a substandard medical school. They said that they were perfectly willing to do their share in improving themselves in the care of their patients. We started by inviting them to our staff meetings, which are purely educational, and to our clinical pathological conferences, which likewise are purely educational. They all came regularly, every one of them. Our staff attendance increased. It was better than we ever expected it would be. Enthusiasm about the staff meetings increased. The members of the active and consulting staffs were put on the spot clearly to show how good they were to these men who had not had so good an opportunity as they had had. I am sure that our hospital has increased its efficiency in the medical care of the citizens of Waltham and its educational value to all the physicians practicing in that community. I know of several lives that have already been saved because these men were able to get critically ill patients into a good hospital immediately. One of our rules was that every one of these men should make application for membership in the Massachusetts Medical Society at the earliest possible moment. Some of them are not eligible because they have not been licensed five years in this state, and those men of course are the ones who need help most. The men who have been practicing for five, ten or fifteen years perhaps do not need so much help as those who are just out of one of these inferior schools. We have taken them all in and have carefully supervised their work.

Give them all an equal chance and then, if you find that they are not satisfactory as members of your supervised courtesy staff — and that is what we call them — you can drop them, that is your privilege. But I do not believe that you will. The tendency will be to improve the teaching all the time, and they will improve all the time and the care of their patients will steadily improve, and as the result you will have a community receiving better hospital care. You will also have a community of effort in the raising of funds. You can imagine in Waltham, for instance, with twelve doctors not allowed to use the hospital and with perhaps ten or twelve thousand of the population, since they are the patients of these doctors, not being able to use our hospital, how disunited we became when attempting to raise funds for the hospital. This past fall, however, the Waltham Hospital attempted to raise \$100,000 to increase the efficiency of the institution, we raised it immediately with a united public effort, and I am sure that it was at least in part due to the operation of this plan, which everybody in the community greets with great pleasure.

I was certain from the beginning that the American College of Surgeons and the Council on Medical Education and Hospitals of the American Medical Association would not disagree with our plan. How could they? They could not disagree with something that was going to benefit the public. And that is the argument that we used in the Legislature in all the legislative bills this year. We have proved to the legislators that we are not after anything — we are simply out to give the people of this state the best possible medical care.

(Dr. Gallupe's remarks were greeted with applause.)

Dr. Nathaniel W. Faxon, Suffolk, in addressing the Council on this subject, spoke as follows:

This is in the nature of a testimonial to Dr. Gallupe's plan and Dr. Phippen's report, and partly in answer to Dr. Schadt's question.

Three years ago a young man from the South Shore who was a graduate of the Middlesex School applied for a residency at the Massachusetts General Hospital. He was investigated very carefully, and it was felt that he had the right stuff in him. He was given an appointment as a resident in anesthesia. He served for two years. He demonstrated his ability and his willingness to work hard and to learn. He is now a member of the paid anesthesia staff at the Massachusetts General Hospital, and we are very glad to have him. This is a direct successful application of the principle. I do not know whether he is a member

of the Massachusetts Medical Society or not. I do not know whether he has been out of Middlesex long enough to be a member. But I do know that he has made good, and I have every confidence that he will continue to be a credit to the hospital and to the medical profession.

(Dr. Faxon's remarks were also applauded.)

The motion to accept the report was adopted by vote of the Council.

Committee to Confer With the Massachusetts Farm Bureau Federation — Dr. Joseph C. Merriam, Middlesex South, chairman.

This report, which is as follows, was presented by the chairman:

This committee was appointed on October 17, 1945. It communicated, forthwith through the chairman, with the Massachusetts Farm Bureau Federation, and received an answer to the effect that there were no immediate problems of the Bureau regarding rural medicine, but that there undoubtedly would arise from time to time matters about which they would wish to confer. The Bureau was assured of this committee's interest and willingness to give them any service they could.

Several communications were received from the committee on Rural Medicine of the American Medical Association, from the American Farm Bureau Federation and from certain midwestern and southern state associations. This literature was carefully studied.

It is the opinion of this committee that whereas there is great need for improvement in rural medical facilities in certain areas of the country, Massachusetts does not present these problems to any great degree. The committee, however, feels that Massachusetts should support the national work and be ready to help its own state farm agencies when and if it is requested by them to do so.

Dr. Merriam moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Representative of the Massachusetts Medical Society on the Massachusetts Committee for Nurses Procurement and Assignment Service — Dr. Dwight O'Hara, Middlesex South.

Dr. O'Hara reported as follows:

The Massachusetts Committee for Nurses Procurement and Assignment Service of the War Manpower Commission, was established by Congressional action in June of 1943. The Massachusetts Medical Society was represented in its deliberations from May, 1944, until it was dissolved on December 31, 1945. Up to September 1, 1945, the Service had classified 9812 nurses, most of whom were of military age. In all 4867 nurses were assigned from Massachusetts, 1146 of them being assigned between January 1 and August 1, 1945. The personnel of the state committee was as follows: Katharine E. Peirce, Mary E. G. Bliss and Hilga Nelson, chairmen; Mrs. Lloyd D. Brace, Dorothy J. Carter, Nathaniel W. Faxon, M.D. (representing the Massachusetts Hospital Association), Mrs. Bessie P. Hanson, Blanche A. Harman, Katherine F. McCahe, Dwight O'Hara, M.D. (representing the Massachusetts Medical Society), Helen O. Potter and Eva S. Waldron. This committee handled a difficult assignment in a creditable manner, serving without compensation and in complete co-operation with all other wartime needs. It is a pleasure to report to the Council the effective work thus done by the nurses of the Commonwealth.

The President asked the Secretary for such comment as the Executive Committee wished to make regarding the report. The Secretary replied that the Executive Committee recommended that this representation be abolished.

It may be desirable at some time in the near future to check up and see what is being done by the several hospitals of the Association and a meeting at that time may be profitable.

Should, however, you desire an earlier meeting I feel sure it can be arranged though it will be in the next administration for my term ends this month.

Sincerely yours,

(Signed) GEORGE A. MACIVER, M.D. President
Massachusetts Hospital Association

The committee will give further consideration as to what should be done to acquaint hospital staffs with the action of the Council.

In discussing this report, Dr Phippen referred to the last sentence in the report proper. He said that, in furtherance of the promise contained in this sentence, the committee had sent a letter to the staffs of all the hospitals in the Commonwealth stating the following:

The enclosed plan was adopted by the Council of the Massachusetts Medical Society on February 6, 1946, and was referred to the Committee to Meet with the Massachusetts Hospital Association. The trustees of the Massachusetts Hospital Association have unanimously agreed to co-operate, and its constituent members have been so informed. The committee therefore requests that you present this plan to your staff and urge its adoption.

Since that time, Dr Phippen continued, the committee had received the following letter from the American College of Surgeons:

AMERICAN COLLEGE OF SURGEONS
40 East Erie Street
Chicago 11, Illinois

Dr. Walter G. Phippen, Chairman
Committee to Meet With the
Massachusetts Hospital Association
31 Chestnut Street
Salem, Massachusetts

April 12, 1946

My dear Doctor Phippen:

Acknowledgment is made of your letter of March 29 relative to the actions and recommendations of the Massachusetts Medical Society and the Massachusetts Hospital Association on graduates of nonapproved medical schools.

The acceptance of interns and residents who are graduates of nonapproved medical schools is the responsibility of the governing body of the hospital in this the American College of Surgeons does not advise or interfere. However, as the American Medical Association approves hospitals for the training of interns, it is advisable that this matter be taken up with that organization in order that there will be no misunderstanding on this subject.

The great trouble with graduates from nonapproved medical schools is the fact that they lack the fundamental education for the practice of medicine and in most instances take the minimum hospital training following graduation, and this usually to a hospital not approved for internships and residencies. We have found case after case in our surveys of hospitals where graduates of these schools, after one year internship in unrecognized hospitals, were attempting to do everything in surgery, obstetrics and highly specialized fields of medicine.

As to the appointment of graduates of nonapproved medical schools to the medical staff of the hospital this is likewise the prerogative of the governing body of the hospital, in co-operation with the proper committee of the active medical staff. Neither the American College of Surgeons nor any other organization may usurp this authority. The American College of Surgeons through its hospital standardization program requires that the professional work of these physicians be under adequate supervision and control and that the privileges extended to them in the hospital be consistent with their qualifications. In order that the welfare of the individual patient will be assured. When these principles of hospital standardization are adequately heeded there is no hazard to the rating of the hospital from this aspect.

Trusting that the foregoing will be of value to you and assuring you of our continued interest and co-operation I am

Very sincerely yours

(Signed) MALCOLM T. MACEachern, M.D.
Associate Director

Dr Phippen also read into the record the following letter, received from the Council on Medical Education and Hospitals of the American Medical Association:

AMERICAN MEDICAL ASSOCIATION
COUNCIL ON MEDICAL EDUCATION AND HOSPITALS
535 North Dearborn Street, Chicago 10

Office of the Secretary
April 24 1946

Dr. Walter G. Phippen
31 Chestnut Street
Salem, Mass.

Dear Doctor Phippen:

At the request of Dr. Victor Johnson, secretary of the Council, I wish to acknowledge your letter of March 29.

The plan which you enclosed would seem to be a logical method of supervising work of registered physicians who do not yet hold hospital appointments. At the same time, it will enable the medical staff to determine the professional competence of individual physicians particularly in relation to subsequent staff appointments and assignment of hospital privileges in various fields of practice. The method which your committee has proposed is similar to many respects to the accompanying statement which has been forwarded to several hospitals in the New England area and also to the Massachusetts Medical Society.

Sincerely yours,

(Signed) F. H. ARZSTAD, M.D.

* * *

The Council on Medical Education and Hospitals is interested in guarding against hospital staff appointments to physicians lacking in professional competence. In its standards, therefore, it has indicated that appointments should be limited to graduates of approved medical schools who have satisfactory qualifications as to training, licensure and ethical standing.

If the graduates of other medical schools wish to obtain the privilege of hospital appointment, their qualifications should likewise be evaluated on the basis of credentials, training and experience in medical practice. It would seem essential, therefore, that such applicants should have a sufficient period of service in the community to enable the medical staff to determine their professional competence. Their applications should then be considered on the basis of individual merit as in the case of other physicians. In this connection, it is necessary to keep in mind that the primary function of the hospital and its staff is to safeguard the care and welfare of the sick.

Dr Phippen moved the adoption of the report. This motion was seconded.

The Secretary suggested that it might be well to send copies of the letters received from the American Medical Association and the American College of Surgeons to each hospital in Massachusetts because of the assurance given that the status of the hospital participating in the plan would not be unfavorably affected by such participation. This suggestion was referred by the President to the committee.

Dr Schadt asked if graduates of unapproved schools who are members of the Massachusetts Medical Society are to be treated under this plan as graduates of the same type of school who are not members of the Society. He pointed out that the former group have already had a five-year probationary period.

Dr Phippen stated that this was a question that must be answered by each hospital dealing with the individual doctor.

Dr H. Quimby Gallupe, Middlesex South, said that he had promised to put this plan into operation in the Waltham Hospital. He continued as follows:

We have in Waltham twelve physicians registered and practicing who are graduates of substandard schools, and the Executive Committee of the staff of the Waltham Hospital believed that it would be very difficult to differentiate one man from another, in other words that it would be almost impossible to pick out of that group men who were more fitted than others to work with the hospital on this plan. We had the plan adopted by the staff of the hospital and then accepted by the Trustees. The responsibility for the working of the plan was left in the hands of the staff.

Through the Executive Committee we invited these twelve men to come to the hospital to a meeting, where the plan was explained to them, we had written copies of rules that would govern their activities in the hospital and we

tion, and that he be appointed by the Council on proposal by a committee of seven to be named by the President.

The only specific duty, then, of this committee is to select and propose the name of a candidate for this position.

The committee felt that the selection of the right man required a definition of his duties far more precise than is given in the vote of the Council, to the end that his qualities and attainments should be adapted to these duties. They therefore communicated with all the state medical societies and the American Medical Association in order to learn of and profit by their experience, and also asked the officers of our district societies to suggest candidates from among their members. This is not the time to summarize and evaluate the many issues and problems thus brought to light. The committee feels that much of the work of the new director must at first be of an exploratory and tentative character and that its final emphasis and value cannot be predicted. Much will depend on the particular talents which he may bring to his office. It believes that ideally the incumbent should be a physician, a member of the Society, experienced in practice and in early middle life, so that before him may stretch a long career of usefulness, which will steadily increase with his experience. Such a man must of course be on a full-time basis, and receive a salary sufficient to enable him to relinquish the income from a successful practice. His appointment should be terminated on his reaching a prescribed age, as in the case of academic or teaching appointments.

The committee has failed thus far to discover a suitable candidate with all these qualifications. They agree that the selection of the candidate is a matter of paramount importance and have preferred to proceed with caution rather than to run the risk through haste of committing a grave error. This report, therefore, is one of progress and contains no recommendation.

Dr Bagnall moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Other Committees

The President stated that no reports had been received from the standing committees on Ethics and Discipline and Industrial Health, or from the special committees on Council Rules, Maternal Welfare, Medical Advisory to Regional OPA and Rehabilitation. Each of these committees had reported at least once during the last year, in accordance with Section 1, Chapter VII of the By-laws. No report had been received from the Committee on Expert Testimony during the preceding year, but this committee received special consideration at the Council meeting on February 6. The question was on the acceptance of a report of no report from each of these several committees.

A motion to this effect was made, seconded and carried.

Committee on Nominations — Dr Ralph R. Stratton, Middlesex East, chairman

Dr Stratton reported as follows

The Committee on Nominations of the Massachusetts Medical Society met on April 3, 1946, at 8 Fenway, Boston, and submitted the following list of officers for the year 1946-1947

President DWIGHT O'HARA, Middlesex South
President-Elect EDWARD P. BAGG, Hampden
Vice-President ISSAC S. F. DODD, Berkshire
Secretary MICHAEL A. TIGHE, Middlesex North
Treasurer ELIOT HUBBARD, JR., Middlesex South
Assistant Treasurer NORMAN A. WELCH, Norfolk
Orator LELAND S. MCKITTRICK, Suffolk

The President asked for nominations from the floor. There were none. A motion was made to close all nominations. The motion was seconded, and it was so ordered by vote of the Council.

Dr Stratton moved that the Secretary be instructed to cast one ballot for the list of officers as submitted by the Committee on Nominations. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary stated that he had complied with this directive, and the President announced that the above mentioned officers were elected.

The President then introduced Dr Dwight O'Hara, president of the Massachusetts Medical Society for the year 1946-1947, who addressed the Council as follows

My professional life has been blessed with many opportunities and many honors. The opportunities I am sure I have not risen to, and the honors I am sure I have not deserved, but this is, I am also most sure, the greatest opportunity and the greatest honor that has been bestowed upon me, and I shall try to do all that I possibly can to be deserving of it. Thank you.

Dr Stratton was appointed by the President to escort Dr Edward P. Bagg, Hampden, president-elect, to the platform. On being introduced to the Council, Dr Bagg spoke as follows

Gentlemen, now you know what the trouble is with your nominating councilors. They have held office too long, and their judgment is uncertain. I will do the best I can, but I must say, if the rules become mixed up with poetic license, it is your fault, and not mine. I was not consulted, gentlemen.

At this point in the meeting the President spoke as follows

Before calling on the President-Elect to fulfill his duty, the chair desires to make a final gesture. He wishes to remind the Council of an interesting bit of history.

The by-laws adopted in April, 1782, state that the Librarian shall have in his custody and charge all books belonging to the Society and shall cause each to be marked on the inside cover with the arms of the Society. On June 7, 1821, the Librarian was further directed to cause the name of the donor to be inserted in each volume.

The chair suggests that each incoming presiding officer of the Council should make his first official appearance with some appropriate ceremony. In this connection there are, he thinks, two insignia of the Society that should be passed in the presence of the Council from one presiding officer to the next.

The first comprises the annual proceedings of the Council for the previous ten years. Their careful study is required by all chairmen.

Each of these eleven volumes before you has been duly marked on the inside cover with the Society's bookplate prepared in 1782, and in accordance with the Council's wish of 1821, has the name of the donor inserted — the President who presided at the first meeting of the Council in that calendar year after his election.

The second is the chairman's copy of *Robert's Rules of Order*, also duly marked with the Society's bookplate. Without this well known guide, no chairman can hope to fulfill his specified duty of presiding at the meetings of even so considerate and tolerant a body as the Council.

Mr Secretary, as retiring chairman of the Council, I now turn back to your hands the volume of the proceedings of the Council for 1935. Dr O'Hara, these insignia are now yours to guard during the one hundred and sixty-sixth year of the Society's life.

Dr O'Hara moved the acceptance of the report and the adoption of the recommendation of the Executive Committee. This motion was seconded, and it was so ordered by vote of the Council.

Representative to the Mental Health for Victory Organization — Dr Abraham Myerson, Norfolk

In the absence of Dr Myerson, the Secretary read the following report, which had been submitted by Dr Myerson:

I think that the Council should be informed that the Mental Health for Victory Organization was "as idle as a painted ship upon a painted ocean." I went to one meeting. No other meetings were called, so far as I know, and nobody did anything at all about it. In fact, nothing could have been done.

I am sorry that the report has to be as futile as it is, but that is the way things went, and I am giving you a candid report.

The Secretary moved the acceptance of the report. This motion was seconded.

The President asked the Secretary for such comment as the Executive Committee might wish to make regarding this report. The Secretary replied that the Executive Committee recommended that this representation be abolished.

The question, as put by the President, was that the report be accepted and the recommendation of the Executive Committee be adopted. It was so ordered by vote of the Council.

Representative to the Legislative Committee of the Massachusetts Central Health Council — Dr William E Browne, Suffolk

The report, as submitted by the chairman, is as follows:

Your representative has attended one meeting of the Legislative Committee of the Massachusetts Central Health Council during the past year. He believes that the Society should continue to have representation on this committee. The Massachusetts Central Health Council has great potentialities and deserves co-operation from the Society.

Dr Browne moved the acceptance of the report. The motion was seconded, and it was so ordered by vote of the Council.

Committee on Postgraduate Assembly — Dr Leroy E Parkins, Suffolk, chairman

Dr Parkins submitted the following report:

A program subcommittee has been established to cover broadly the fields of medicine and surgery. An executive subcommittee has been established including representatives from the other New England states in order that the assembly may continue to be the New England Postgraduate Assembly rather than a local one. The committee anticipates that the assembly will be held in the fall and that choice of date and arrangements of the details of the program will soon be completed. This report is submitted for information and makes no recommendation.

Dr Parkins supplemented this report by saying that the Assembly would be held on October 30 and 31, 1946, at a place not yet determined. He added that, during the course of the assembly, there would be

a symposium on the care of the veteran throughout the English-speaking world.

Dr Parkins moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Representative to the Hospital Council of Boston — Dr William E Browne, Suffolk

The following report was offered by Dr Browne:

Your representative has attended one meeting of the Hospital Council of Boston during the past year. At this meeting the general problem of professional charges to ward patients in hospitals was discussed. In certain hospitals no charges are made for the professional care of such patients, and in other hospitals, under certain conditions, a charge for such services is regarded as proper. The problem was presented whether any rule on this matter could be formulated. Your representative expressed the opinion that the establishment of any general rule should not be attempted, the problem varied so much in each hospital as to make it seem wise to leave the affair in the hands of the hospital and to encourage each hospital to establish such policies in the matter as best met its own needs.

Your representative believes that the Society should continue to have representation on this Council. In this way can the viewpoint of the practicing physician — the most important component part of the Society — be kept before a group of individuals especially interested in broad hospital problems.

Dr Browne moved the acceptance of the report. This motion was seconded, and it was so ordered by vote of the Council.

Representative to the Massachusetts Nursing Council for War Service — Dr David D Scannell, Norfolk

The following report was offered by Dr Scannell:

During the past two years your representative has been notified of three meetings of the Council, which he attended. The Council now plans to change its name to the Greater Boston Nursing Council and to continue under a new constitution and by-laws. Since representation to the Massachusetts Nursing Council for War Service appears no longer necessary, your representative respectfully requests his discharge from this position.

Dr Scannell moved the acceptance of the report. This motion was seconded.

The President called on the Secretary for such comment as the Executive Committee might wish to make regarding this report.

The Secretary replied that the Executive Committee recommended that this representation be abolished.

The question, as put by the President, was on the acceptance of the report and the adoption of the recommendation of the Executive Committee. It was so ordered by vote of the Council.

Committee of Seven Appointed to Nominate a Director of Medical Information and Education — Dr Elmer S Bagnall, Essex North, secretary

The report, which is as follows, was offered by Dr Bagnall:

The Council of the Society voted on October 3, 1945, that a new position be created whose incumbent shall be known as the director of medical information and educa-

The treasurer of the Society, Dr Ehot Hubbard, Jr., compared the expenditures of the Society during the last three years. He said that in 1944 they were \$38,544, in 1945, \$42,537, and that in 1946 the hudget stood at \$60,000. He expressed it as his helief that at least an increase of \$5 per year was necessary if the Society was to continue with plans already laid out. Dr Hubbard also expressed it as his belief that, should an increase in dues be ordered, an increased allocation of funds should be made to the distinct societies.

Dr Walter G. Phippen, president of the Boston Medical Library and a member of the Executive Committee from Essex South District Medical Society, expressed himself as in favor of the proposed increase, believing that of the \$20.00 so collected, \$5.00 should be allocated to the Library for the purpose of making it possible for this institution to serve the physicians of Massachusetts better. He said that, although the Library was most anxious to enlarge its scope of benefits, it found itself in such a financial position as to preclude this possibility.

The allocation of \$5.00 per member would make it possible for the Library to serve what it regards as its real purpose.

Dr Phippen, in speaking of the historical aspects of the Library, said that it was instituted in 1805. He said that it was the third largest medical library in the United States, with nearly 200,000 volumes and 135,000 pamphlets. The value of the Library contents he estimated as probably more than one million dollars.

He said it should be a modern research library, with modern conveniences for study. It should have a well-trained staff of sufficient size to give expert bibliographical aid to all members of the profession, to students and to research workers. This function it cannot perform because it has grown so fast that it has outgrown its financial means to do so.

Dr Phippen said that the present income of the Library is about \$30,000 per year and that an additional \$30,000 is needed.

He pointed out that in a survey of the Library in 1941, Thomas F. Fleming, medical librarian of Columbia University, indicated that the future of the Library hinged on its development as a reference library not only for the benefit of Boston but also for that of the rest of Massachusetts and New England.

Dr Phippen expressed the thought that if the books, which now more or less clutter up certain rooms, might be properly stacked, these rooms might become available for Society committee purposes.

The Secretary moved the adoption of the recommendation. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary read the following letter addressed to the President:

AMERICAN ACADEMY OF PEDIATRICS
MASSACHUSETTS STUDY OF CHILD HEALTH SERVICES
319 Longwood Avenue Boston
Telephone BEAcon 3911

April 18 1946

Dr Reginald Fitz, President
Massachusetts Medical Society
8 The Fenway
Boston Massachusetts

Dear Dr Fitz:
Following up our conversation of last week, I should like to ask you or someone you might appoint to sit on the Advisory Committee of our study. It is planned that the committee will meet twice at the most and the first meeting will be on Wednesday, May 1, at the DuBarry Restaurant, 159 Newbury Street, at 12:30 p.m.

Sincerely yours,
(Signed) LEADON SVEDEKER
Executive Secretary

Under the rules, the President referred this communication to the Committee on Public Relations.

The Secretary read the following letter from Dr George F. Lull, secretary of the American Medical Association:

April 9, 1946

TO THE SECRETARIES OF THE CONSTITUENT STATE MEDICAL ASSOCIATIONS

The Committee on National Emergency Medical Service of the American Medical Association, which was appointed in accordance with recommendations of the Board of Trustees adopted by the House of Delegates at its meeting held in December, 1945, has requested the Board of Trustees to give them permission to suggest that each constituent state medical association appoint a similar committee. This request has been approved by the Board. The recommendation adopted by the House of Delegates is as follows:

The Board of Trustees would recommend to the House of Delegates that it authorize the Board of Trustees of the American Medical Association to appoint a committee of seven to be known as the Committee on Military Service. This committee shall include four civilian physicians who served in the war and three others. The committee will study the many communications that have been received and the suggestions made by physicians in the armed forces. The committee will also formulate policies for recommendations to be forwarded through the Surgeons General to the Secretary of War and the Secretary of the Navy expressing the views of the medical profession in planning for proper utilization of the services of physicians in any national emergency.

The Chairman of the Committee, Dr. Edward L. Bortz, of Philadelphia, desires that as much publicity as possible be given the formation of these committees.

Very truly yours
(Signed) GEORGE F. LULL

This letter was referred by the President to the Committee on Postwar Planning.

Dr Charles J. Kickham, Norfolk, was recognized. He stated that, during one of the committee meetings of the Massachusetts Medical Society, the subject of revising upward the salaries of the Society's employees had been considered. He expressed his opinion that the rising cost of living had made such revision necessary in all walks of life. He discussed the various ways in which such a revision might be brought about.

Dr Peirce H. Leavitt, Plymouth, expressed himself as believing that, if increases in salary were authorized, such increases should be made retroactive to a certain date.

The part that the Committee on Finance played in such a proposal was discussed.

Dr Kickham finally moved that the President be authorized to appoint a special committee of three to confer with the Committee on Finance and subsequently to report the matter through the usual channels, with the idea of making any change in salaries retroactive to a certain date, if it so deemed wise. The motion was seconded, and it was so ordered by vote of the Council.

Dr Bagnall was recognized. He spoke as follows:

It appears that the time may soon come when a change in income level of those eligible for the standard Blue Shield service contract may become necessary. It would seem prudent for the Society to be ready with factual data on this subject.

He moved that the President be authorized to appoint a special committee of five for this purpose. The motion was seconded, and it was so ordered by vote of the Council.

On a motion by a councilor, which was seconded by another, the Council voted to suspend the rules so as to provide Dr Norman A. Welch with the opportunity of presenting to the Council an informational report on the Blue Shield.

Dr Welch spoke as follows:

Before Dr McCann left for California, he asked me as one of the directors of the Blue Shield, if I would present to you some information about this organization and I

Dr O'Hara replied as follows

I am sure that Dr Fitz has gone as far as anyone could, farther than I would have believed anyone could have, to ease the way and smooth the path in the legislative manner with these relics which he now hands on to me. I only hope that I may be able to approach his pattern of diligence and behavior and preparation. Those of you who know how hard Dr Fitz has worked know what a tremendous job he has done for the Society through a very difficult year. My endeavor will be to follow as nearly as I can I know many reasons why I will not be able to keep up with his example, but as nearly as I can, I shall follow the pattern that he has placed before you.

The President-Elect submitted a list of nominations to committees for the year 1946-1947. It was moved and seconded that the nominations be confirmed. It was so ordered by vote of the Council. (The members of the standing and special committees for the year 1946-1947 will appear in the proceedings of the Society in the September 19 issue of the *Journal*.)

NEW BUSINESS

The following letter from the President was received by the Secretary

Dr Michael A Tighe, Secretary
Massachusetts Medical Society
8 Fenway
Boston 15, Massachusetts

April 3, 1946

Dear Mr Secretary

Since the aims of both Blue Cross and Blue Shield have the support of the Society and since our employees are in no way protected by Social Security, may I suggest through you to the Executive Committee and the Council that henceforward the Massachusetts Medical Society adopt as a policy the payment of annual subscriptions to Blue Cross and Blue Shield for each person in our employment.

Yours sincerely,

(Signed) REGINALD FITZ, M.D., President
Massachusetts Medical Society

The Secretary said that the Executive Committee had reviewed this communication and recommended that the Council authorize the enrollment mentioned. He moved the adoption of the recommendation. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary read the following letter sent by the President to Dr Francis C Hall, chairman of the Committee on Finance, and the latter's answer.

Dr Francis C Hall, Chairman
Committee on Finance
372 Marlboro Street
Boston, Massachusetts

April 3 1946

Dear Francis

Because of the urgency of the situation I am writing you at this late date requesting an extraordinary appropriation. The clerical work of the Society is increasing by leaps and bounds. To meet such needs, which I believe are entirely proper, I hereby request an extraordinary appropriation of \$3500 to be used for the employment of secretarial help.

Yours sincerely,

(Signed) REGINALD FITZ, M.D., President
Massachusetts Medical Society

April 4 1946

Dr Reginald Fitz, President
Massachusetts Medical Society
8 Fenway
Boston, Massachusetts

Dear Reg

I have your letter requesting an extraordinary appropriation of \$3500 for the employment of secretarial help to be used under the direction of Dr Tighe to take care of the increased activities of the Massachusetts Medical Society.

Of course there has been no time to call a meeting of the committee and discuss this in detail, but I am not sure that the committee would feel differently if we did discuss it. I have talked with Dr William Dr O'Brien and Dr Johnson, all members of the Committee on Finance. Dr Bancroft Wheeler will be out of town until tomorrow so that I was unable to talk with him. Those of us who have discussed the matter believe that the President and Secretary know the needs of the Society and have the interests of the Society at heart.

We therefore feel that we have no choice but to express our confidence in them and endorse their request for this extraordinary appropriation. Therefore, the Committee on Finance hereby approves this appropriation, understanding that it will be submitted to the Executive Committee and Council for approval.

Cordially yours,

(Signed) FRANCIS C. HALL, M.D., Chairman
Committee on Finance

The President called on the Secretary for such comment as the Executive Committee might wish to make regarding these communications.

The Secretary stated that the Society had but one full-time clerk, that the amount of clerical work in connection with the Society's business had increased by leaps and bounds and that the present setup was no longer adequate.

He emphasized the fact that two additional permanent clerks were needed. Reference was also made to the facts that in the past certain clerks in the employ of the *Journal* had been utilized on Society's business, that this had ceased to be a satisfactory arrangement, that reports were delayed beyond the time when they were most effective, and finally that much clerical work had to go for completion to outside secretarial offices, at great expense.

The Executive Committee recommended that the Council authorize this appropriation.

The Secretary moved the adoption of the recommendation. This motion was seconded, and it was so ordered by vote of the Council.

The Secretary, acting under the direction of the Executive Committee, made the following recommendation:

That the Council authorize the President to appoint a committee of five for the purpose of studying the question of raising the annual membership dues of the Massachusetts Medical Society and, in the event that such an increase is deemed necessary, for the further purpose of studying what part, if any, of the increase should be allocated to the Boston Medical Library.

The Secretary offered the following explanatory statement in support of the recommendation:

At a regular meeting of the Executive Committee held on January 9, 1946, a motion was made and seconded that the committee recommend to the Council that, beginning in January, 1947, the membership dues in the Massachusetts Medical Society be raised to \$20.00 per year. This subject was debated at length at that time. The subject was finally laid on the table until the next regular meeting of the committee.

During the interval between the meeting of January 9 and the one held on April 24, the President addressed each member of the Executive Committee with a request that he ascertain the reaction of the members of his district toward this proposal.

Some districts conducted a postcard survey in this matter, in others the sentiment of their respective districts was checked by word of mouth in casual contact.

The members of the Executive Committee, while expressing themselves as believing that the mounting expenses of the Society made such a move necessary, did not believe that they were sufficiently informed as to the general sentiment of the Society to make a specific recommendation to the Council along these lines.

APPENDIX NO 2

TREASURER'S REPORT

The year 1945, being the last of the war years, saw a further drop in income from dues to \$40,825 from \$41,215 in 1944. And through the canceling of the annual meeting the customary income from the Committee on Arrangements was not realized. However, a very pleasant increase occurred through the operations of the *New England Journal of Medicine* in the form of a return of \$22,800, which is not to be added to General Fund principal but to be used as income for expenditures in 1946. The Society has a right to feel proud of the continued increase in circulation enjoyed by the *Journal* under Dr Nye's management, maintained this year under rather unfavorable circumstances for production.

It is also pleasant to announce the repayment of the \$25,000 loan made by the Society to the Massachusetts Medical Service in 1942. This repayment was as of December 31, 1945, and contributes toward the relatively large cash balance reported at the end of the year, as well as toward the reduced total value of securities held in the General Fund as compared with 1944. This sum will be invested early in 1946.

In 1945, \$1312 was received for subscriptions to the *Journal* from members in service and was made over to the *Journal* as in 1944.

The income from the Building Fund securities has been added to the Building Fund principal in contrast to the procedure followed in 1944 but in line with the custom adhered to for many years previous.

The General Fund securities stand at a book value of \$142,689 and market value of \$149,353 as compared to \$167,614 and \$170,885 respectively for 1944.

The Building Fund securities for 1945 amount to \$68,027 book value and \$73,270 market value as compared to \$68,170 and \$70,858 respectively for 1944.

Endowment Fund securities have a book value of \$23,166 which remains the same as in 1944.

Income from the General Fund was \$4527 with a yield of 3.17 per cent as compared with \$3969 in 1944. Income from the Building Fund was \$2156 with a yield of 3.17 per cent as compared with \$1960 in 1944.

Profit on securities sold, called or matured, in the General Fund was \$991 and in the Building Fund was \$173.

During the year there was no change in the portfolio of the Endowment Fund securities. Changes in the General and Building funds came mostly through bonds called or matured, to replace which one issue of convertible preferred stock was bought together with \$44,500 United States Treasury 2½ per cent bonds maturing in 1972-1967, which already have a market value well above their purchase price. The Society now holds a total of \$87,900 in government bonds throughout the different funds.

Total revenue for 1945 was \$71,434 and total expenses were \$42,538, leaving an excess of revenue over expenses of \$28,896.

Total Building Fund assets amount to \$70,537, an increase of \$2330 over last year. General Fund assets amount to \$211,199, an increase of \$30,122 over last year. Endowment Fund assets remain at \$23,166, causing the Society to end 1945 with a grand total of \$304,903 assets in cash and securities, an increase of \$32,452 over 1944.

The Treasurer would like to point out recent trends in the Society's activities that cause changes in the financial picture. From the point of view of revenue, the largest factor is the healthy growth of the *Journal* emerging from a stage not many years ago when the Society was called upon to advance money to help promote its efforts. From the viewpoint of expenditures certain committees are largely expanding the scope of their work in the interest of education of the profession and promotion of the health and protection of the community. Barring unforeseen and extreme fluctuations in these two factors, and in anticipation of increased income from dues as members return from the services, and from the re-establishment of the annual meeting, he believes that a balance can be maintained safely from year to year, on the present basis.

He would like again to acknowledge his great indebtedness to his secretary for her incomparable aid in the function of his office and to express gratitude for the helpful assistance rendered by the entire staff of the *New England Journal of Medicine*.

A breakdown of comparative expenses for 1944 and 1945 is appended

	1944	1945
Salaries		
Secretary	\$3,000 00	\$3,000 00
Executive Secretary	3,000 00	4,000 00
Treasurer	2,000 00	2,000 00
Expenses		
President	714 36	608 77
Secretary	2,195 00	3,189 87
Treasurer	2,113 04	1,968 74
Delegates to A M A	779 40	818 86
Maintenance of Society Headquarters	6,538 64	3,746 33
Shattuck Lecture	200 00	0
Cotting Luncheons	358 50	504 20
Committees		
Arrangements	0	272 15
Ethics and Discipline	159 07	143 20
Executive	463 52	287 74
Finance	16 90	20 23
General Administrative	0	2,509 80
Industrial Health	97 61	92 87
Information Bureau	1,135 02	2,942 48
Legislation	204 80	3,580 02
Massachusetts Hospital Association	0	08
Maternal Welfare	1 58	3 16
Medical Advisory to OPA	7 85	0
Medical Defense	1,115 05	571 67
Medical Education	89	0
Membership	76 96	125 70
Military Postgraduate	411 06	607 63
Obstetrics and Gynecology	0	0
Postgraduate Instruction	4 60	0
Postwar Loan Fund	92 60	466 44
Postwar Planning	103 36	2,440 84
Postpayment Medical Care	44 90	8 66
Prepaid Medical Care	116 00	0
Public Health	24 28	82 36
Public Relations	164 06	1,295 05
Rehabilitation	0	44 10
Rules	0	4 51
Tax-Supported Medical Care	0	47 21
Wagner Bill Conference	56 03	0
War Participation	209 61	34 29
New England Medical Council Publications	0	100 00
<i>New England Journal of Medicine</i>		
Directories	7,900 00	0
Refunds to district societies	51 36	1,709 00
Refunds to fellows on active service	4,000 00	4,000 00
<i>New England Journal of Medicine</i> for subscriptions to <i>Journal</i> from Fellows in active service	28 00	0
Net loss on securities, sold, called or matured	1,164 00	1,312 00
	0	0
	\$38,544 33	\$42,537 96

ELIOT HUBBARD, JR., Treasurer

APPENDIX NO 3

REPORT OF THE EXECUTIVE COMMITTEE

The Executive Committee of the Council reviewed all the reports contained in the circular of advance information. It noted that they were to be a large extent informational. Beyond recommending their acceptance by the Council, the committee took no action. The committee also noted, however, that certain of these reports contained recommendations and it is with these that this report will deal specifically.

Committee on Arrangements

This committee recommends that all fellows be urged to visit the commercial exhibits during the course of the annual meeting. The Executive Committee, recognizing

promised that I would. So in spite of the fact that the time is late, I will keep my promise, but I shall be brief.

At present there are approximately 275,000 participants in the Blue Shield program, and this number is increasing at the rate of 20,000 a month. This compares with 220,000 at the beginning of the year.

The plan for the additional medical care in the hospitals has been completed and I believe has received the approval of the Insurance Commissioner, through whose office all these additions to the contract must go.

Considering the national pressure for very extensive coverage of the prepayment plans, the directors of the Blue Shield have approved the plan to increase the Blue Shield field, not only to add medical coverage in the hospitals, but also to add surgical coverage in outpatient departments, homes, and offices.

The actuary of the Blue Shield and the Blue Cross feels that there will be a slight increase in rates required to cover the surgical care in the home, office and outpatient department, and this will be accomplished by an increase in the rate from 85 cents to 95 cents for a single individual, from \$1.65 to \$1.90 for a married couple, and from \$2.00 to \$2.25 for a family.

Dr. McCann is, of course, very enthusiastic about the extension of coverage to include surgery in the home, office and outpatient department.

He also wanted me to mention to the Council, although I believe this has appeared in the Treasurer's report, that the Blue Shield has returned to the Massachusetts Medical Society the \$25,000 which was advanced by the Society when this plan was formulated.

(Dr. Welch's statement was greeted with applause.)

There being no further business before the Council, the President declared the meeting adjourned at 10:15 p.m.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO. 1

ATTENDANCE OF COUNCILORS

BERKSHIRE

I. S. F. Dodd
Solomon Schwager
Helen M. Scoville
P. J. Sullivan

BRISTOL NORTH

W. H. Allen
J. H. Brewster
W. J. Morse
J. L. Murphy
W. M. Stobbs

BRISTOL SOUTH

G. W. Blood
R. B. Butler
H. E. Perry
C. C. Tripp
Henry Wardle

ESSEX NORTH

E. S. Bagnall
R. V. Baketel
Elizabeth Councilman
H. A. Fenton
E. H. Ganley
H. R. Kurth
P. J. Look
R. J. Neil
R. C. Norris
G. L. Richardson
F. W. Snow
C. F. Warren

ESSEX SOUTH

Bernard Appel
D. S. Clark
R. E. Foss
Loring Grimes
P. P. Johnson
A. E. Parkhurst
O. S. Pettingill
W. G. Phippen
E. D. Reynolds
H. D. Stebbins
P. E. Tivnan
C. F. Twomey

FRANKLIN

J. E. Moran

HAMPDEN

F. H. Allen
E. P. Bagg
E. C. Dubois
P. E. Gear
Frederic Hagler
G. D. Henderson
Charles Jurist
A. G. Rice
G. L. Schadt
J. A. Seaman

HAMPSHIRE

H. A. Tadgell

MIDDLESEX EAST

J. L. Anderson
Richard L. Dutton
R. W. Layton
M. J. Quinn
W. F. Regan
R. R. Stratton

MIDDLESEX NORTH

D. J. Ellison
A. R. Gardner
W. F. Ryan
M. A. Tighe

MIDDLESEX SOUTH

E. W. Barron
I. M. Baty
G. F. H. Bowers
Madeline R. Brown
R. N. Brown
R. W. Buck
E. J. Butler
J. F. Casey
C. W. Clark
H. F. Day
C. L. Derick
J. G. Downing
H. Q. Gallupe
V. A. Getting
H. G. Giddings
H. W. Godfrey
J. L. Golden
A. D. Guthrie
Eliot Hubbard, Jr.
F. R. Jouett
A. A. Levi
A. N. Makechnie
J. C. Merriam
C. E. Mongan
J. P. Nelligan
E. J. O'Brien, Jr.
Dwight O'Hara
Fabyan Packard
L. G. Paul
S. H. Remick
Max Ritvo
E. H. Robbins
E. W. Small
H. P. Stevens
A. B. Toppan
C. F. Walcott
A. L. Watkins
Hovhannes Zovickian

NORFOLK

C. E. Allard
B. E. Barton
Carl Bearse
Arthur Berk
M. I. Berman
G. L. Doherty
Susannah Friedman
J. B. Hall
H. B. Harris
R. J. Heffernan
P. J. Jakmauh
I. R. Jankelson
C. J. Kickham
C. J. E. Kickham
D. S. Luce
C. M. Lydon
D. L. Lynch
F. P. McCarthy
H. L. McCarthy
R. T. Monroe
F. J. Moran
Hyman Morrison
D. J. Mullane
J. J. O'Connell

W. R. Ohler
G. W. Papen
S. A. Robins
D. D. Scannell
L. A. Sieracki
S. L. Skvirsky
Kathleene S. Saow
J. W. Spellman
W. J. Walton
N. A. Welch

NORFOLK SOUTH

D. L. Belding
F. W. Crawford
Frederick Hinchliffe
E. K. Jenkins
N. R. Pillsbury
D. B. Reardon

PLYMOUTH

A. L. Duncombe
P. H. Leavitt
C. D. McCann
G. A. Moore
E. L. Perry
W. H. Pulsifer

SUFFOLK

W. J. Brickley
W. E. Browne
A. M. Butler
A. J. A. Campbell
N. W. Faxon
Reginald Fitz
Joseph Garland
R. L. Goodale
F. C. Hall
John Homans
A. A. Hornor
L. M. Hurxthal
C. S. Keefer
H. A. Kelly
R. I. Lee
W. J. Mixer
H. L. Musgrave
H. F. Newton
R. N. Nye
F. R. Ober
J. P. O'Hare
L. E. Parkins
Helen S. Pittman
J. H. Pratt
W. H. Robey
H. F. Root
R. M. Smith
M. C. Sosman
J. J. Todd
S. N. Vose
Conrad Wesselhoeft
C. F. Wilnsky

WORCESTER

C. R. Abbott
B. H. Alton
A. W. Atwood
George Ballantyne
F. P. Bousquet
W. J. Elliott
John Fallon
L. M. Felton
W. F. Lynch
R. S. Perkins
R. J. Ward
R. P. Watkins
B. C. Wheeler

WORCESTER NORTH

C. B. Gay
J. V. McHugh

fact that in the past certain clerks in the employ of the *Journal* have been utilized on Society's business, that this has ceased to be a satisfactory arrangement, that reports are delayed beyond the time when they are most effective and finally that much clerical work has to go for completion to outside secretarial offices involving considerable expense. The Executive Committee recommends that the Council authorize this appropriation.

Dues

At a regular meeting of the Executive Committee held on January 9, 1946, a motion was made and seconded that the committee recommend to the Council that, beginning in January, 1947, the membership dues in the Massachusetts Medical Society be raised to \$20.00 per year. This subject was debated at length at that time. The subject was finally laid on the table until the next regular meeting of the committee.

During the interval between the meeting of January 9 and the one held on April 24, the President addressed each member of the Executive Committee with a request that he ascertain the reaction of the members of his district toward this proposal.

Some districts conducted a postcard survey in this matter, in others the sentiment of their respective districts was checked by word of mouth in casual contact.

The members of the Executive Committee, while expressing themselves as believing that the mounting expenses of the Society made such a move necessary, did not believe that they were sufficiently informed as to the general sentiment of the Society to make a specific recommendation to the Council along these lines.

The treasurer of the Society, Dr. Eliot Hubbard, Jr., compared the expenditures of the Society during the last three years. He said that in 1944 they were \$38,544, in 1945, \$42,537, and that in 1946 the budget stood at \$60,000.

He expressed it as his belief that at least an increase of \$5.00 per year was necessary if the Society was to continue with plans already laid out. Dr. Hubbard also expressed it as his belief that, should an increase in dues be ordered, an increased allocation of funds should be made to the district societies.

Dr. Walter G. Phippen, president of the Boston Medical Library and the member of the Executive Committee from Essex South District Medical Society, expressed himself in favor of the proposed increase, believing that of the \$20.00 so collected, \$5.00 should be allocated to the Library for the purpose of making it possible for this institution to serve the physicians of Massachusetts better. He said that, while the Library was most anxious to enlarge its scope of benefits, it found itself in such a financial position as to preclude this as a possibility.

The allocation of \$5.00 per member would make it possible for the Library to serve what it regards as its real purpose.

Dr. Phippen, in speaking of the historical aspects of the Library, said that it was instituted in 1805. He said that it was the third largest medical library in the United States with nearly 200,000 volumes and 135,000 pamphlets. The value of the Library contents he estimated as probably more than one million dollars.

He said it should be a modern research library with the modern conveniences for study. It should have a well-trained staff of sufficient size to give expert bibliographic aid to all members of the profession, students and research workers. This function it cannot perform because it has grown so fast that it has outgrown its financial means to do so.

Dr. Phippen said that the present income of the Library is about \$30,000 per year and that an additional \$30,000 is needed.

He pointed out that in a survey of the Library in 1941, Thomas F. Fleming, medical librarian of Columbia University, indicated that the future of the Library hinged on its development as a reference library not only for the benefit of Boston but also for that of the rest of Massachusetts and New England.

Dr. Phippen expressed the thought that if the books, which now more or less clutter up certain rooms, might be properly stacked, these rooms might become available for Society committee purposes.

The Executive Committee, under the head of new business, will recommend that the Council authorize the Presi-

dent to appoint a committee of five for the purpose of studying the question of raising the annual membership dues of the Massachusetts Medical Society and, in the event that such an increase is deemed necessary, for the further purpose of studying what part, if any, of the increase should be allocated to the Boston Medical Library.

MICHAEL A. TIGHE, *Secretary*

APPENDIX NO 4

REPORT OF THE COMMITTEE ON MEDICAL EDUCATION

On October 17, 1945, the Council referred to this committee the following resolution, offered by Dr. Charles E. Morgan:

WHEREAS, The question has been repeatedly asked in public and private concerning the facilities for medical education in Massachusetts, and

WHEREAS, No satisfactory scientific answer has been forthcoming, therefore, be it

RESOLVED, That the Massachusetts Medical Society undertake a survey of medical educational facilities at present available in New England.

The committee has held several meetings, has consulted with the deans of several medical schools, the head of the state departments of health, other educational officials here and in the American Medical Association, and now begs to submit the following informational report.

There are five medical schools in the six New England states approved by the Approving Authority of the Commonwealth of Massachusetts. They are as follows:

	REGISTRATION OVER
Yale University School of Medicine New Haven Conn.	200
Boston University School of Medicine Boston Mass.	210
Harvard Medical School Boston Mass.	530
Tufts College Medical School Boston Mass.	410
University of Vermont College of Medicine Burlington Vt.	125
Total Registration	1475

It seems unnecessary to describe the educational facilities of these schools as to buildings, hospital affiliations, endowment, annual budgets, faculties and so forth. This information for the most part is available in the printed catalogues of the schools, which can be had on request to their deans. Their facilities are sufficient to warrant the continued approval and support of their parent university.

Medical education is expensive. The tuition fees, usually ranging from \$400 to \$600 per student per academic year, cover only a fraction of the actual cost, the rest is borne by endowments, grants from the parent organization, philanthropic and charitable foundations, or by federal, state and community funds. For comparison with the cost of other educational processes, note the following table taken from the "Educational Number" of the *Journal of the American Medical Association* for January 13, 1940.

SCHOOL	COST PER STUDENT CREDIT HOUR
Education	\$4.06
Commerce	5.92
Engineering	10.52
Law	11.05
Agriculture	14.51
Dentistry	15.87
Medicine	26.96

It is reasonable to assume that these figures would be greater today.

The high cost to the student can be offset to some degree by scholarships and grants and by part-time extracurricular employment, an expedient which is undesirable in that it takes energy from the main task of studying medicine.

Are these five schools able to create enough doctors to meet the medical needs of New England adequately? This is hard to answer, for what is adequate? Of course, New England should not be considered as a unit independent of the rest of the country, for there is a free inter-

the growing importance of these exhibits in the success of the annual meeting, approves of this recommendation and, in the furtherance of its objective, recommends additionally that the *New England Journal of Medicine* carry suitable reference to these exhibits and that the several chairmen who preside over the exercises of the annual meeting be instructed to call, at least twice daily, the attention of the gathering to them and to the importance of paying them a visit

Committee on Medical Education

This report, in a special manner, elicited the commendation of the Executive Committee. It is an excellent factual study of correlated material brought together from many sources. Its conclusions are soundly drawn. The Executive Committee was aware that the stimulus to the resolution offered by Dr Mongan, by which the Council authorized this study, largely came about as the result of inquiry by members of the Massachusetts Legislature regarding the need of additional medical schools in Massachusetts.

Because this report now makes such information readily available, the Executive Committee, in addition to recommending that this report be accepted by the Council, further recommends that the Council specifically direct the attention of the Committee on Legislation to it for such use as this latter committee may deem wise.

In so directing the attention of the Committee on Legislation to this report, the Executive Committee points out that Table 4 as it relates to the rejections, without explanation, might be subject to serious misunderstanding.

The Executive Committee would have the Council and the Committee on Legislation know that most candidates apply simultaneously to many medical schools and that those rejected by one school frequently find places in others. The Executive Committee has it on authority that a little over 50 per cent of all applicants find places in some medical school.

Committee on Public Health

The Executive Committee notes that this report contains the following recommendation: "That the president of the Society be authorized to take the initiative in aiding the four district societies concerned in selecting suitable representation on the Greater Boston Nursing Council."

The Executive Committee disapproves of this recommendation. It believes that, because of the Society's statewide character, it should not associate itself with an organization that is purely sectional in its scope and purpose.

The Executive Committee recommends that the Council reaffirm its stand in this matter as taken on October 6, 1937.

The Executive Committee further recommends that the Council instruct the Secretary to write to Miss Tracy, of the Greater Boston Nursing Council, advising her of the Society's sympathetic interest in this matter and recommending that she make contact with the district societies concerned.

Committee on Public Relations

The Executive Committee noted that this report contained one recommendation and a reference, without recommendation, to a correlated matter.

The recommendation would have the Council approve of the enrollment of the members of the Society in the Blue Cross in such a manner as is considered most efficient by the Secretary and the officials of the Blue Cross. The Executive Committee approves of this recommendation and recommends its adoption.

The Executive Committee noted that this report contained a reference to a similar enrollment of the members of the Massachusetts Medical Society in the Blue Shield. It also noted that the Committee on Public Relations was unwilling to take a stand on this matter because of the possible involvement of one of the Society's traditions whereby one physician cared for another or another's dependents without charge.

In the discussion attending this subject before the Executive Committee, Dr Milton Quinn was heard. He believed that many members of the Society were overburdened by the care of other physicians and their families. He saw

no reason why individual members of the Society might not join the Blue Shield if they so desired. The question at issue, as he defined it, was whether or not the Massachusetts Medical Society should endorse their joining.

In connection with the subject, Section 2, Article II, of the "Principles of Medical Ethics" of the American Medical Association was read into the record. This section reads as follows:

When a physician from a distance is called on to advise another physician or one of his family dependents, and the physician to whom the service is rendered is in easy financial circumstances, a compensation that will at least meet the traveling expenses of the visiting physician should be proffered. When such a service requires an absence from the accustomed field of professional work of the visitor that might reasonably be expected to entail a pecuniary loss, such loss should, in part at least, be provided for in the compensation offered.

It was pointed out that at least inferentially, except under the circumstances outlined, this section indicates that it is not considered good medical ethics for one physician to charge another for services rendered.

The Executive Committee offers no recommendation regarding this matter.

Committee on Legislation

The Executive Committee believes that the Committee on Legislation acted with wisdom regarding the matters outlined in its report.

Massachusetts Delegates to the Council of the New England State Medical Societies

The Executive Committee directs the attention of the Council to a typographical error occurring in this report, "1946" should read "1945."

The Executive Committee recommends, subject to the approval of the Committee on Finance, that the sum of \$100 be set aside to cover the expenses of the Council, a like amount being contributed by each of the state medical societies concerned.

Representative of the Massachusetts Medical Society on the Massachusetts Committee for Nurses Procurement and Assignment Service

The Executive Committee recommends that this representation be abolished.

Representative of the Massachusetts Medical Society to the Mental Health for Victory Organization

The Executive Committee recommends that this representation be abolished.

Representative to the Massachusetts Nursing Council for War Service

The Executive Committee recommends that this representation be abolished.

Nominations

The Executive Committee reviewed certain committee nominations made by the President-Elect for the year 1946-1947 and recommends their approval by the Council Communications.

The Executive Committee reviewed a communication concerning an enrollment of the employees of the Society in the Blue Cross and Blue Shield. The communication was received by the Secretary and signed by the President. The Executive Committee recommends that the Council authorize this enrollment.

The Executive Committee reviewed a communication addressed to Dr Francis C Hall, chairman of the Committee on Finance and signed by the President, and Dr Hall's answer. In this communication, the President requests an extraordinary appropriation of \$3500 to be used for additional secretarial help in the Society's offices. In supporting this appropriation, the President pointed out that the Society has but one full-time clerk, that the amount of clerical work in connection with the Society's business has increased by leaps and bounds and that the present setup is no longer adequate to meet our needs. It was emphasized that two additional permanent clerks are needed at the present time. Reference was made to the

Table 4 shows the rejection rates for applicants to the medical schools in this area in a recent six-year period. The total number of candidates varies greatly, the number accepted (one fifth to one half) remains constant for a

TABLE 2 Number of Applicants to Medical Schools in New England in the Years 1935-1942 *

		SINGLE APPLICATION	MULTIPLE APPLICATION	TOTAL APPLICANTS
Massachusetts	1935	180	335	515
	1936	161	303	464
	1937	137	329	466
	1938	144	276	420
	1939	108	263	371
	1940	151	272	423
	1941	157	245	402
Connecticut	1942	189	248	437
	1935	58	114	172
	1936	64	113	177
	1937	59	113	172
	1938	75	113	188
	1939	44	126	172
	1940	51	105	156
Rhode Island	1941	57	98	155
	1942	48	152	200
	1935	20	50	76
	1936	8	56	64
	1937	19	47	66
	1938	20	46	66
	1939	16	54	70
Maine	1940	17	39	56
	1941	13	35	48
	1942	14	32	46
	1935	29	36	65
	1936	19	39	58
	1937	10	33	43
	1938	21	21	42
New Hampshire	1939	13	35	48
	1940	12	25	37
	1941	13	23	36
	1942	14	27	41
	1935	26	31	57
	1936	17	21	38
	1937	18	19	37
Vermont	1938	21	13	34
	1939	21	19	40
	1940	20	21	41
	1941	20	29	49
	1942	14	23	37
	1935	51	7	58
	1936	60	8	68
	1937	44	10	54
	1938	47	10	57
	1939	31	10	41
	1940	44	16	60
	1941	29	12	41
	1942	30	7	37

*Figures obtained from the Educational Numbers of the Journal of the American Medical Association

given school according to its capacity, and a few less are finally enrolled. It would be unwise to create enough medical schools to take care of all who now apply to enter them. The law of supply and demand seems to have settled on a proper

TABLE 3 Proportion of Medical Students Who Are Educated in Their Native State or in New England for the Years 1937-1944 *

	STUDENTS IN NATIVE STATE	STUDENTS IN OTHER N. E. STATES	TOTAL STUDENTS	PERCENTAGE N. E. STUDENTS IN N. E. SCHOOLS
United States	112 412		193 186	56
Connecticut	360	454	2088	35
Massachusetts	4145	347	6963	64
New Hampshire	44	264	746	41
Vermont	688	62	892	84
Maine		377	838	45
Rhode Island		414	898	46
New England	5237	1918	12 425	57

*Figures obtained from the Educational Numbers of the Journal of the American Medical Association

ratio of physicians to population in this country, as shown in Table 1. To increase this to any large extent would be costly and not in the interests of the public welfare. We do not need more doctors, we need better doctors, rather

than a flood of mass-produced and hence inferior doctors. We must conclude on such evidence that New England does not now need a new medical school, and that its present schools can meet the medical needs of the anticipated growth in population in this area for the next several years. Were any new school to be developed, we believe that it could be placed more advantageously and usefully

TABLE 4 Fate of Applicants to the Six New England Medical Schools in the Years 1938-1942 *

		APPLICANTS ACCEPTED	APPLICANTS REJECTED	TOTAL APPLICANTS	ENROLLED
Yale	1938	91	454	545	55
	1939	77	427	504	54
	1940	71	418	489	—
	1941	64	417	481	50
	1942	66	540	606	58
Harvard	1938	152	696	848	124
	1939	151	668	819	128
	1940	146	579	725	—
	1941	144	581	725	117
	1942	147	703	850	147
Tufts	1938	133	255	388	100
	1939	138	270	408	104
	1940	132	251	383	—
	1941	141	195	339	111
	1942	146	316	462	111
B U	1938	96	294	390	57
	1939	102	319	421	64
	1940	89	356	425	—
	1941	109	266	375	69
	1942	128	420	548	63
Dartmouth	1938	22	135	157	22
	1939	20	104	124	20
	1940	23	162	185	—
	1941	23	122	145	22
	1942	29	62	91	24
Vermont	1938	34	32	66	32
	1939	32	35	67	32
	1940	32	54	86	—
	1941	33	55	88	33
	1942	38	62	100	36

*Figures obtained from the Bulletin of the Association of American Medical Colleges

in Maine or Connecticut than in Vermont, Rhode Island or Massachusetts.

ROBERT T. MONROE, Chairman

APPENDIX NO 5

REPORT OF THE COMMITTEE ON PUBLICATIONS

The Committee on Publications has secured Dr. John B. Youmans, associate professor of medicine at Nashville, Tennessee, and recently serving as a colonel in the Medical Corps of the United States Army and chief of the Nutrition Branch of the Office of the Surgeon General in Washington, to deliver the Shattuck Lecture at the annual meeting of the Society in 1946.

The Directory of Fellows has been printed and distributed in accordance with the vote of the Council.

The accounts of the Journal have been audited by Hartsorn and Walter and found to be in order. An abstract of this report is appended and copies of the full audit have been filed with the Treasurer and the Committee on Finance.

The committee has continued to supervise the publication of the New England Journal of Medicine. The Journal has prospered under the able direction of the managing editor, Dr. Robert N. Nye, with the assistance of Miss Davies, the associate editors and the members of the Editorial Board. The Society has reason to be proud of what has been accomplished. In reporting to the Council this phase of the committee's duties we quote from the report made by Dr. Nye to the committee:

During 1945, the New England Journal of Medicine experienced its best year under ownership by the Massachusetts Medical Society. The circulation continued to increase and, because of this, operations were profitable. New subscriptions for the year totaled slightly less than those for 1944, the respective figures being 5913 and 6109. On the other hand, cancellations were fewer in 1945 than in 1944, so that the net increase in circulation was the largest in the history of the Journal. As of December 31, Journals were being sent to 4398

change of students. And the question should be separated as much as possible from issues such as distribution of physicians and volume of student applications.

It would seem reasonable to assume that if the proportion of physicians in the population over a fair number of years remains stable, that proportion is probably acceptable ("adequate") in terms of public need. If it rises, increased need would appear to have been felt and met, if it falls, the saturation point must have been reached.

On this assumption, the sample figures in Table 1 were assembled from the *American Medical Directory*, the *Year Book of Facts* and the reports of the United States Census. It is seen that, over a period of twenty-four years, the population of the United States increased over 26,000,000; the number of physicians increased over 41,500, but that

TABLE 1 Proportion of Physicians in the Population of the United States and New England

	POPULATION (APPROX.)	NO. OF PHYSICIANS	PHYSICIANS PER 1000 POPULATION
1918 United States	105,000,000	147,812	1.408
Massachusetts (1916)	3,662,339	5869	1.607
(Boston)	729,600	2018	2.770
(Springfield)	103,200	201	1.929
Connecticut (1916)	1,223,583	1678	1.371
(New Haven)	147,000	266	1.811
(Hartford)	108,900	256	2.331
New Hampshire (1916)	440,584	690	1.567
(Concord)	22,400	44	1.964
Maine (1916)	767,638	1205	1.569
(Portland)	63,014	165	2.624
Rhode Island	602,765	772	1.282
(Providence)	250,000	432	1.727
Vermont	362,452	668	1.845
New England	7,059,361	10,882	1.541
United States	106,418,284	145,608	1.370
Massachusetts	3,852,356	5959	1.548
(Boston)	747,900	2095	2.800
Connecticut	1,380,000	1729	1.253
(New Haven)	162,300	318	1.960
New Hampshire	443,000	641	1.447
Maine	768,014	1105	1.438
Rhode Island	604,397	778	1.287
Vermont	352,400	594	1.686
New England	7,400,000	10,806	1.462
United States	122,775,046	156,440	1.275
Massachusetts	4,249,600	6595	1.552
(Boston)	781,100	2549	3.268
(Springfield)	149,900	262	1.748
Connecticut	1,606,900	2165	1.349
(New Haven)	162,600	438	2.695
New Hampshire	465,200	567	1.209
Maine	797,400	989	1.240
(Portland)	70,800	167	2.364
Rhode Island	687,400	844	1.228
(Providence)	252,900	527	2.083
Vermont	359,800	489	1.360
New England	8,166,300	11,649	1.426
United States	126,425,000	165,163	1.307
Massachusetts	4,335,000	7263	1.675
(Boston)	781,100	2770	3.546
(Springfield)	149,900	295	1.968
Connecticut	1,655,000	2401	1.470
(New Haven)	162,600	486	2.994
New Hampshire	470,000	593	1.262
Maine	804,000	966	1.201
(Portland)	70,800	161	2.272
Rhode Island	705,000	924	1.310
(Providence)	252,900	566	2.247
Vermont	361,000	503	1.394
New England	8,330,000	12,650	1.519
United States	131,669,000	189,496	1.443
Massachusetts	4,316,000	8085	1.876
(Boston)	770,800	2934	3.717
(Springfield)	149,500	296	1.980
Connecticut	1,709,000	2720	1.602
(New Haven)	160,600	528	3.289
New Hampshire	491,500	687	1.398
Maine	847,200	1011	1.194
(Portland)	73,600	166	2.252
Rhode Island	713,300	958	1.344
Vermont	359,200	551	1.536
New England	8,436,200	13,012	1.543

the number of physicians for each thousand persons changed very little, — from 1.408 in 1918 to 1.443 in 1942. Expansion of medical educational facilities has kept even pace with increase in population. Therefore, it would appear that this proportion of physicians is about what the public asks for, at least at its present level of appreciation of need.

New England has a higher ratio of physicians to population than the rest of the country in every sampled year.

In 1918, it had 1.541 physicians per thousand population; in 1921, it had 1.462, in 1931, it had 1.426, in 1936, it had 1.519, and in 1942, it had 1.543. Massachusetts persistently has had a higher ratio of physicians to population than any other New England state except for Vermont in 1918. Their uneven distribution between towns and cities, however, is plain — in Boston greatest of all, perhaps because it is the chief center of medical education for the area.

Another fact that emerges from Table 1 is that the states which have medical schools maintain a higher proportion of physicians than those which do not. This has been true of Massachusetts and Vermont for many years. Connecticut had a low physician ratio in 1918 and 1921 but attracted more doctors than population thereafter. On the other hand, Rhode Island has been low in physicians in ratio to population in four of the five sampled years and equaled the national average only once, and Maine has been low every year.

Finally, Table 1 suggests that there is no present need for the establishment of a new medical school in Massachusetts, or even in New England. Harvard and Yale being national schools, take large numbers of students from beyond New England, but Tufts, Boston University and Vermont give distinct preference to in-state and New England residents.

As the population of New England increases, more physicians must be trained. At some time in the future, therefore, the question must be faced whether it will be better to expand the existing educational plants or to arrange for the development of one or more new schools. Various considerations will have to be weighed carefully, such as the financial expense, the ideal size of a medical school, the existent clinical facilities, and the needs of the community. The conclusions of the Council on Medical Education and Hospitals as published in the *Journal of the American Medical Association* for September 1, 1945, show much common sense. A few are quoted.

Any overall increased present or postwar need for additional physicians occasioned by the war can be provided by existing approved schools. There is no justification for establishing new medical schools for this purpose. Furthermore, the normal annual number of graduates from existing schools is adequate for the peacetime needs of the country, granted distribution is equal.

The maldistribution of physicians as between the states or between urban centers and rural areas is a problem to be attacked primarily by other means than the production of more doctors in a given state, the rate of production and the distribution of doctors in this country are independent.

Medical education is by far the most expensive form of professional training, requiring an initial outlay and subsequent annual budgets in the early years totaling millions of dollars and not tens or hundreds of thousands. A school whose resources include annual budgets of less than \$350,000, independent of the cost of maintenance of the hospital and out-patient departments, is unlikely to conduct a satisfactory program.

The medical educational facilities in New England and all over the country are inadequate in the opinion of the college student, for there are only about half as many places in schools as there are applicants for them. Dr. Fred C. Zappfe's annual reports in the *Bulletin of the Association of American Medical Colleges* show, for the years 1933-1942, applicants varying from 11,800 to 14,043, with 50 per cent acceptances. Many candidates seek to assure themselves of a place by applying to several schools at once. The figures of recent years for our territory are shown in Table 2. The volume of applications does not show a significant upward trend, though there is a suggestion that it decreases in good business years and increases in bad years.

Table 3 shows that New England takes care of the same proportion of its students wishing to enter medicine as does the rest of the country. Massachusetts and Vermont do distinctly better than that. Connecticut students go in greatest number to nearby New York. Students from our two states without medical schools show a slight preference for schools outside of New England.

Pharmaceutical Association and the New York State Medical Society and State Board of Pharmacy, regarding existing laws and regulations bearing on harbiturates, sulfonamides, penicillin and so forth

We find that under federal law, harbiturates cannot be sold without a doctor's prescription. Refills may be dispensed by the druggist unless the doctor has otherwise directed. The active director informs us that with only about two hundred inspectors to cover the whole field of food, drugs and cosmetics, there can be no adequate coverage of the practices of fifty thousand retail drug-stores. He expresses the hope that because this is primarily a local problem, the drug industry will concern itself with corrective measures. The druggist would like the co-operation of the medical profession particularly by stating on the prescription whether or not and how many times refills are authorized in each instance. "N R" would mean no refills.

In New York City and New York State, there are regulations under the law which are aimed at controlling abuses. In Massachusetts there appears to be opinion that legislation is needed, but there is not yet agreement that the public interest would be best served by seeking legislation now.

The new labeling regulations under the federal law have just become effective and it was agreed at a conference on December 17, 1945, that we should await the experience under that regulation before taking action in this state. This conference included the Commissioner of Health, the secretary of the Board of Registration in Pharmacy, the president and legal counsel of the Massachusetts Pharmaceutical Association and our committee. The pharmacists expressed their gratification for this co-operation in approaching solution of mutual problems.

ELMER S BAGNALL, *Chairman*

APPENDIX NO 7

REPORT OF THE COMMITTEE ON POSTWAR PLANNING

Postgraduate courses planned by the Subcommittee on Postgraduate Medical Education have been conducted throughout the State as follows:

District No 2 — Springfield, Holyoke, Northampton and Greenfield — two courses

District No 3 — Worcester, Gardner, Fitchburg and Leominster — two courses

District No 4 — Lowell, Haverhill, Lawrence and Newburyport — two courses

District No 5 — New Bedford, Fall River and Hyannis — one course

District No 6 — Beverly, Salem, Lynn, Danvers and Gloucester — five courses

District No 7 — The Greater Boston Area. In this area a comprehensive postgraduate lecture course, open to every licensed physician in the Commonwealth, meeting each Monday and Wednesday, has been in progress since February 18 and will continue to May 15, 1946. Over a thousand doctors have registered for this course and to date the average attendance at each meeting has exceeded five hundred.

In District No 1 — Pittsfield, North Adams and Wilmamstown — courses are in preparation.

Through the efforts of the subcommittee on Veterans' Affairs information has been obtained in regard to the need of returning medical veterans for office space, industrial opportunities, assistantships, hospital facilities for the care of their patients and opportunities for a return to practice. Replies to a questionnaire submitted at the postgraduate course in Cambridge indicated that there is no urgent need at present for taking any active steps to secure office space for doctors. Physicians willing to share their offices temporarily might be listed at the headquarters of the Society. Any older physicians wishing a young doctor as an assistant may also find help at 8 Fenway through the Bureau of Clinical Information. All returning physicians are concerned about the impossibility of getting telephone listings before December when the new directory is issued. Information regarding the efforts which the New England Telephone Company is making to aid

this problem will be published in the *New England Journal of Medicine*. It is apparent that there will be a need for the continued and enlarged activities of the Bureau of Clinical Information at 8 Fenway to give aid to returning veterans for a period of several years. The questionnaire sent out by the American Medical Association in relation to opportunities for physicians has not been properly filled out by all the eighteen district societies with the result that at 8 Fenway inadequate information is available for those doctors seeking information about opportunities for practice in various parts of the State.

Conference with officers of the Massachusetts Hospital Association was held with regard to providing hospital appointments for veterans.

HOWARD F ROOT, *Chairman*
LEROY E PARKINS, *Secretary*

APPENDIX NO 8

REPORT OF THE COMMITTEE ON LEGISLATION

The committee, representing the eighteen district societies, has had two meetings. In order to facilitate action it has delegated powers to a small executive subcommittee, which has held four additional meetings. Mr Charles J Dunn has been appointed legislative counsel.

Federal activities have been chiefly confined to Senate 1606 and its satellite bills. Dr Reginald Fitz was appointed to represent the Committee on Legislation at the legislative hearings at Washington in co-operation with Dr Elmer S Bagnall, the representative of the Council of the Massachusetts Medical Society. Later, at the request of Dr Joseph S Lawrence, of the American Medical Association, a special committee of five — Drs Reginald Fitz, Elmer S Bagnall, Michael A Tighe, Dwight O'Hara and James C McCann — was appointed to handle all federal legislation. Senator Murray stated recently that it would not be possible for state medical societies to be heard at these hearings, but that they were invited to submit statements in writing. Such a statement, embodying the views of the Massachusetts Medical Society, has been sent to Senator Murray.

The usual perennial bills with a sprinkling of new ones have been presented to the Massachusetts Legislature. Your committee has reviewed some sixty-nine bills relative to medicine and public health, and has voted to approve thirteen, to oppose fifteen, and to take no action on forty-one. Most of these bills have now been heard before their respective legislative committees. At the hearings on important bills the Massachusetts Medical Society has been represented by its legislative counsel, by the chairman of the Committee on Legislation or by selected speakers.

The present status of some of the more important bills is as follows. The adverse reports of the legislative committees on the bills on antivaccination and the special board of osteopathy have been accepted by the Legislature. A special committee, with members from the three medical schools and hospitals, ably handled the anti-vivisection bills. A resolve to set up a recess committee to investigate animal experimentation, which was substituted for the adverse report of the Committee on Legal Affairs on H R 117, was defeated by a narrow margin in the Senate. The two other antivivisection bills have not as yet come up for final disposal by the Legislature. The bill for reciprocity with other states in licensing physicians has been favorably reported and is now before the Ways and Means Committee.

At the present time bills relative to the following subjects are still in the legislative committees: (1) changes in the requirements for admission to examinations for license to practice medicine, (2) revocation of charters for nonfunctioning and poorly functioning medical and osteopathic schools, (3) the opening of hospitals to any licensed physician, and (4) the establishment of a special chiropractic board.

The Committee on Legislation has considered two matters referred to it by the Council at its meeting on February 6, 1946.

members of the Massachusetts Medical Society, 362 members of the New Hampshire Medical Society, 9766 regular subscribers, 3263 medical students and 299 miscellaneous readers, — a grand total of 18,088 copies, which represents an increase of 3203 for the year.

During 1945 the *Journal* received no money from the Society except those sums paid to the treasurer for subscriptions to the *Journal* by members in the armed forces. In spite of this, cash on hand as of December 31, 1945, amounted to \$28,977. A check for \$22,800 was turned over to the treasurer of the Society.

During 1945, the editorial board considered 203 manuscripts, of which 129 were accepted for publication. The corresponding figures in 1944 were 194 and 151.

Last fall all limitations on paper were removed. This was fortunate, since the allotted tonnage for the fourth quarter would not have sufficed and an ex-quota allowance over and above that already granted would have been necessary. Since then, the weight of the paper has been increased from forty to fifty pounds, more coated stock has been used, and the pagination has been increased. By the end of 1946, it is hoped that the grade of paper will improve and that the pagination can be increased to the prewar level.

Difficulties regarding printing of the *Journal* still exist. Although at one time last summer copies of certain issues were placed in the mail within a day or so of the date of publication, the spread gradually increased, and at the end of the year copies were being received about two weeks after the date of publication. Furthermore, the delivery of reprints has been held up to such an extent that it is difficult to appease the authors. The delay in printing the *Journal* is due partly to failure to deliver copy according to schedule and to last-minute changes, and partly to difficulties in the printing plant — one of the latter being the time required to run through issues that contain three or four different colors in the advertising pages. It is hoped that these matters can be adjusted during the current year. The press-work continues to be excellent.

With the increase in circulation, particularly at a time when the addresses of those in the armed forces are continually changing, the time required to handle the mailing list is the major item of the office staff. Undoubtedly this will taper off as physicians adopt permanent residences, but at the moment it necessitates almost superhuman effort. To this has been added an increasing amount of work for officers and committees of the Society, and, in spite of adding one girl to the office staff, Miss Davies and her assistants are still overwhelmed. That they are able to complete what they are asked to do is a miracle, and for this they again deserve the highest commendation.

Although the *Journal* can function during 1946 with the space now available, additional room *must* be provided by 1947. If the rooms now occupied by the Society were obtainable, space would be ample.

The outlook for 1946 appears excellent, so far as the editorial department of the *Journal* is concerned. More papers are being submitted for publication, which will permit the editorial board to be somewhat more critical in their acceptance than it has in the past two or three years. On the other hand, the cost of publishing the *Journal* will markedly increase, largely owing to an increase in the per-pound cost of paper and an approximate 50 per cent increase in tonnage, due to heavier stock and increased pagination. This increase will be somewhat offset by higher advertising rates, but it seems likely that, with the cancellation of the 90 per cent excess profits tax, many of the pharmaceutical houses will curtail their advertising programs. Although the circulation will undoubtedly increase, the increases of the past two years cannot be expected. Consequently, although the *Journal* will probably continue to be profitable, a sum of \$5000 has been requested in the current budget.

JAMES P. O'HARE
CONRAD WESSELHOEFT
OLIVER COPE
JOHN FALLON
RICHARD M. SMITH, *Chairman*

NEW ENGLAND JOURNAL OF MEDICINE ABSTRACT OF AUDITOR'S REPORTS

	1943	1944	1945
Current Assets			
Cash	\$6,151 52	\$6,148 53	\$6,176 71
Accounts Receivable	7,222 39	7,166 12	9,153 86
Capital Assets	960 85	1,213 64	1,146 35
Totals	\$14,334 76	\$14,528 29	\$16,476 94
Current Liabilities	172 21	407 50	605 10
Surplus	\$14,162 55	\$14,120 79	\$15,871 84
Expenses			
Publication of <i>Journal</i>	\$49,047 02	\$67,609 73	\$76,417 73
Publication of reprints	4,563 96	6,123 72	5,150 41
Office and other salaries	23,885 50	25,480 17	30,458 12
Commissions, fees, etc.	4,116 98	5,478 47	7,893 91
Office and sundry expenses	4,731 21	5,009 32	5,150 61
Totals	\$86,344 67	\$109,701 41	\$125,081 55
Revenue			
Advertising	1943	1944	1945
Engraving	\$34,455 36	\$38,271 40	\$73,852 44
Reprints	1,368 44	1,042 61	974 10
Subscriptions (other than M. M. S.)	3,739 33	4,389 43	6,194 49
Miscellaneous	39,680 53	55,978 15	66,278 18
	1,248 77	2,033 06	2,327 89
Totals	\$80,492 43	\$101,764 65	\$149,627 10
Net loss or profit to M. M. S.	\$5,852 24 (loss)	\$7,936 76 (loss)	\$24,545 75 (profit)
Net publishing cost expenses minus (revenue minus subscriptions)	\$45,532 77	\$63,914 91	\$41,732 41
Average paid circulation	10,420	13,447	16,264
Net cost per subscriber	4 37	4 75	2 50
Net cost per member M. M. S. (based on net loss)	1 30	1 81	—

APPENDIX NO. 6

REPORT OF THE COMMITTEE ON PUBLIC HEALTH

This committee presents herewith the report of Dr. Elmer S. Bagnall's subcommittee which has considered state legislation to control the dispensing of certain drugs.

This report is informational only but well worth the careful reading by every member of the Society.

The President referred to this committee a request from Miss Margaret H. Tracy of the Greater Boston Nursing Council that the Society appoint a representative to sit on their council. The Council of the Massachusetts Medical Society on October 6, 1937, rejected a similar request because it felt that the Massachusetts Medical Society should not, as a state organization, enter into a purely local problem. The Committee on Public Health recognizes the value of public relations and the necessity of approving such projects as may be sponsored by the Greater Boston Nursing Council, inasmuch as they relate largely to problems of medical interest. Your committee feels that it will be much more logical to approve their programs before they are inaugurated and co-operate with the Greater Boston Nursing Council, rather than have no voice in the formation of its policies. Your committee is of the opinion that such procedure will result in better public relations, better understanding and better co-operation with a closely allied profession. The committee therefore recommends that the president of the Society be authorized to take the initiative in aiding the four district societies concerned in selecting suitable representation on the Greater Boston Nursing Council.

There has been some delay in the appointment of the subcommittee to study ways and means to improve the medical health services to the schools.

We hope that before the annual meeting this committee will be in action and ready to report in the fall.

ROY J. WARD, *Chairman*

REPORT OF THE SUBCOMMITTEE TO CONSIDER STATE LEGISLATION TO CONTROL DISPENSING OF CERTAIN DRUGS

Your committee has inquired from the Federal Food and Drug Administration in Washington, the Massachusetts Board of Registration in Pharmacy and the Massachusetts Department of Public Health, as well as the Massachusetts

This was the first meeting in one and a half years — much too long an interval — since so many things of very great importance were required to be discussed and acted on, and it must be remembered that the House of Delegates determines the policy of the American Medical Association and the trustees merely carry these policies out. Incidentally, it was proposed and will be voted in July next to have two meetings of the House of Delegates a year, one at the regular convention time and the other in mid-winter, presumably in Chicago.

There was an unusually good attendance (171 out of 176), really remarkable when one considers the difficulties of traveling and securing hotel accommodations. One comes back always from these meetings with renewed convictions that this is a real medical democracy, without pressure groups or blocs, composed of the very best men from all over the country who have only one thing in mind, the furtherance of medicine.

We went through three really very intense days without any breaks, one got the impression that we were attempting to do rather too much in too short a time. As an explanation of that, however, was the feeling that we were uncertain as to what was the opinion in Washington, when the hearings on the various compulsory sickness insurance bills were coming up, and the collateral lay pressure as shown, for example, in the rather large advertisement in the *New York Times* and other big metropolitan dailies appearing almost simultaneously with our meeting. These advertisements contained the names of three or four hundred prominent people in national life and various large business concerns, all endorsing President Truman's health message. These influences unquestionably had some effect in making the House of Delegates work under pressure.

The usual addresses of the President and the Speaker were read but easily the best address was one given by President-Elect Roger Lee on the second evening of the meeting, the subject being, "What Is Medical Care?" His address deserved a much larger visual audience. I say this without prejudice and uninfluenced by any affection or local pride. In the absence of a large American Medical Association meeting, the audience on the evening of the second day was rather small and the address was not broadcast but it was printed in the December 15 issue of the *Journal of the American Medical Association* and should be read by everyone. As a matter of fact these addresses, those of the President, the President-Elect and the Speaker, should be read by all members. These appear under the minutes of the meeting in the December 15 and 22 issues. Obviously these addresses are much too long to review in even summary.

The organization of the American Medical Association House of Delegates calls for many reference committees, this year fourteen of them. To the reference committees are referred by the Speaker the business matters as they turn up. The members of these committees work long and late, particularly this year. Of our delegates, Walter Phippen was chairman of the important Reference Committee on Medical Care of Veterans, with Leland McKittrick as associate. Also co-operating on that committee was Henry Viets, section on nervous and mental diseases. The report of Dr. Phippen's committee was splendidly done and well received. (At this point I should say that in our opinion there would have been no difficulty whatever in Dr. Phippen's being elected a trustee had he cared to serve, he is well known and highly thought of, and we were prepared to nominate him up to the very last moment had he chosen to stand for election, but he felt that he could not afford the time. In his place Dr. James R. Miller of Hartford, Connecticut, a most able man, was elected without any difficulty.) Dr. Dwight O'Hara served well and conscientiously, as always, on the Committee on Reports of the Board of Trustees and Secretary.

I need not discuss how these reference committees sit in various outside rooms and listen to the pros and cons in any measure that comes up. Suffice to say that the members work conscientiously and well, and it devolves on the chairman of each committee to write up the report of his committee and present it to the secretary after being read in the House of Delegates as a whole. I do not remember, in my experience, that I have ever known reference committees to work as they did on the occasion of this meeting.

Now as to the highlights of our first day the December 1 issue of the *Journal of the American Medical Association* was distributed to the members the day before you received your copies here, with the splendid and logical editorial "The Present National Health Problem and the New Wagner Bill." As said above, almost coincidentally with this meeting a large paid advertisement appeared in the *New York Times* and other metropolitan dailies, obviously having in mind an offset to the meeting of the House of Delegates. There can be no question that these things hung like a shadow over the meeting and made for increased pressure. Unquestionably these various activities accelerated moves to put out voluntary prepaid medical care measures and the correlation and co-ordination of them countrywide to demonstrate what could be done in that way. As we know, there are about fifty-nine different plans for medical service, in twenty-five different states at the present time, and an attempt must be made to get these into some more or less general scheme of efficiency.

Without question the appearance of General Hawley of the Veterans' Administration was most happy and stimulating. He is a wholesome, forthright, understanding and sympathetic man, and his address before the House of Delegates, published in the December 22 issue of the *Journal of the American Medical Association*, deserves most careful reading.

Other things of interest were the following recommendation of the transfer of the Children's Bureau from the Department of Labor to the Public Health Service, organization of a new section on general practice, approval of a national research foundation under the control of a board of directors composed of scientists, recommendation of the appointment of a Medical Cabinet officer, unanimous adoption of a proposal to create a national medical plan to provide voluntary sickness insurance for all Americans at cost, within their means, fostering the development of this insurance in areas where there are none such, the Council on Medical Education and Hospitals of the American Medical Association does not intend to remove any hospital from its list of hospitals approved for internships or residencies which furnishes teaching facilities to any veteran medical officer who is eligible for educational benefits under the Servicemen's Readjustment Act, — provided the veteran is legally eligible for medical licensure in the state in which the hospital is located, and disapproval of Senator Pepper's super-EMIC program, which would have allowed the Children's Bureau to provide free medical care for every United States child under twenty-one and for every United States woman during pregnancy. Also disapproved were those portions of the Wagner-Murray-Dingell bill which would have had the effect of socializing medicine.

The members should read the excellent article "Medical Care for the American" by Dr. Louis Bauer in the December 1 issue of the *Journal of the American Medical Association*. This is a most helpful article and represents a lot of thought on the part of the committee of which he was chairman.

Great pride was felt by all of us in the selection of Dr. George R. Minnt for the Distinguished Service Medal, particularly when only a few years ago Dr. Elliott P. Joslin was the recipient.

George Lull was appointed as assistant to Olin West and probably his successor. Dr. Lull impressed everybody at the meeting with his extremely great capabilities. He is a straightforward, entirely capable man, succeeding, however, a man whom the American Medical Association can badly do without — Olin West. Olin West is a name to most doctors but personally he is a tower of strength to the organization and it will be a sad day when he gets out. His health is not too good and has not been for the last couple of years.

The resignation of Speaker Shoulders was rather dramatic and unexpected. He was promptly nominated, however, for the position of president-elect and in a rather close election beat out E. J. McCormack, of Toledo, Ohio, another extremely able man and a most active member of the House of Delegates, the vote was 77 to 51. Dr. Shoulders has been speaker for many years and is a hard worker and a capable man. Last year you will remember, in order to have Dr. Lee become president-elect, his resignation as a trustee was asked for (by agreement) so that he might

The first was "that the Massachusetts Medical Society send a return postal card to all members of the Society on the Wagner-Murray-Dingell Bill (Senate 1606) requiring a 'yes' or 'no' answer as to whether or not they favored this legislation."

After due discussion, the committee voted not to make a poll of the Massachusetts Medical Society in respect to Senate 1606. The committee believed that such a poll would be ineffective since a previous poll on HR 1328 resulted in only about one fifth of the members voting. Also the results would be misleading because those who favor such legislation would vote, and those who were opposed would be less likely to reply. Furthermore, a divided vote would not strengthen the position in Washington of the representative of the Society, who now has definite instructions from the Council to oppose S 1606.

The second matter referred to the committee by the Council is as follows:

That it is the sense of the councilors of the Norfolk District that a list of the final vote of the Massachusetts Legislature on the Chiropractor Bill of 1945, be published in the *New England Journal of Medicine*, this list to be published by districts rather than alphabetically, and if space is difficult to obtain, that it be published in several successive issues a few districts at a time.

After careful deliberation the committee voted unanimously to disapprove of publishing such a list. It was felt that its publication would seriously interfere with the efforts of the committee in changing the votes of members of the Legislature in respect to this bill, and Mr Charles J Dunn, the legislative counsel for the committee, advised against such publicity as seriously hampering his work.

DAVID L. BELRING, *Chairman*

APPENDIX NO 9

REPORT OF THE MASSACHUSETTS DELEGATES TO THE COUNCIL OF THE NEW ENGLAND STATE MEDICAL SOCIETIES

The Council of the New England State Medical Societies was formed in the summer of 1945. Its organizational meeting was held in Providence, Rhode Island, on July 18, 1945. The Massachusetts Medical Society was represented at this meeting by Dr Dwight O'Hara, president-elect, Dr Allen G Rice and Dr Michael A Tighe, secretary of the Society.

All the state medical societies of New England were represented.

The purpose of the Council, as outlined by the temporary chairman, Dr John F Kenney, of Pawtucket, was to bring about a closer co-operation between the state medical societies of New England in the development and maintenance of the highest standards in the conduct and administration of medical care, in the development of plans relative to the better organization of medicine and in the furtherance of plans to improve the health of all the people in the New England states.

He added that the Council shall not be concerned with the problems that are peculiar to the individual state but shall deal with the larger matters in which all the state medical societies of New England are concerned.

He emphasized the fact that the Council shall not seek to supersede the control now exercised by the governing bodies of each respective state medical society, or that of the House of Delegates of the American Medical Association.

The annual meeting of the Council was set for the third Wednesday in April of each year. Other meetings were provided for at the call of the president of the Council.

It was decided at this meeting that the Council would take no stand on any matter before it unless the will to do so was unanimous.

It was voted that each of the New England state medical societies be asked to support this Council as an experiment for one year by the contribution of one hundred dollars. The method by which the Council would be financed beyond this time was left for a future time.

The following officers were elected to serve until the third Wednesday in April, 1946:

Dr James R Miller, *President*
Dr John F Kenney, *Vice-President*
Mr John E Farrell, *Executive Secretary-Treasurer*

The Council held its second meeting in Providence, Rhode Island, on October 14, 1945.

At this meeting the Council voted to join the New England Council — an organization for the most part concerned with the business interests of New England.

The need for a program by the civilian doctor, whereby the veteran could obtain the medical care to which he was entitled under the law, was discussed.

The importance of informing the public with regard to pending legislation was stressed.

Medical-care plans came under discussion.

The Council met again on February 3, 1946. This meeting was held at 8 Fenway, Boston. The special guests of the Council on this occasion were the president of the American Medical Association and certain members and associates of the Council on Medical Service and Public Relations of the American Medical Association.

The program of this meeting was as follows:

PROGRAM

- 1 15 p m Registration
- 1 30 p m Call to order
Presiding James R. Miller, M D, president, Council of the State Medical Societies of New England trustee, American Medical Association
- 1 40 p m Greetings to Conference
Roger I Lee, M D, president, American Medical Association
- 1 50 p m "The Work of the Council on Medical Service and Public Relations of the American Medical Association"
"Prepayment Medical Care Plans" Mr Jay Keisner, executive vice-president, Michigan Medical Service, chairman, Advisory Committee on Prepayment Medical Care Council on Medical Service and Public Relations.
"Fourteen Point Constructive Program for Medical Care." Louis H Bauer M D member of Council on Medical Service and Public Relations trustee, American Medical Association
- 2 20 p m Discussion
- 2 40 p m "The Returning Veteran and the American Medical Association" Major General George F Lull, M C.
- 3 00 p m Discussion
- 3 10 p m "The Washington Front." Joseph S Lawrence M.D., director of the Washington Office of the Council on Medical Service and Public Relations of the American Medical Association
- 3 30 p m Discussion
- 3 45 p m "The Hill-Burton Bill and the Hospital System" Fitz Arestad, M D, assistant secretary, Council on Medical Education and Hospitals of the American Medical Association. Discussant: Reginald Fitz, M D, member, Council on Medical Education and Hospitals of the American Medical Association president, Massachusetts Medical Society
- 4 15 p m "Round Table Discussion on Public Relations." "Co-operative Community Relationships" W W Bauer, M D, director Bureau of Health Education American Medical Association
"The Job of State and County Societies in Medical Public Relations" C Charles Burlingame, M D chairman Committee on Public Education, American Psychiatric Association chairman Committee on Public Relations Connecticut State Medical Society
- 4 45 p m Discussion
- 5 15 p m Adjournment

ALLEN G RICE
DWIGHT O'HARA
MICHAEL A TIGHE

APPENDIX NO 10

REPORT OF A MASSACHUSETTS REPRESENTATIVE TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION

As one of your members of the House of Delegates at the meeting of the American Medical Association in Chicago from December 1 to 5, 1945, I have the following report to make:

ea where the tissue was somewhat firmer and noother. The terminal bronchi were not visible, wing to obstructing masses of hemorrhagic tissue. A biopsy of the left lower bronchus showed chronic inflammation. A slight hemoptysis occurred four days later, when an x-ray film showed no change. The patient's condition was unchanged after bronchoscopy.

An operation was performed on the sixteenth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. LOWREY F. DAVENPORT. This patient, if the history is accepted at face value, had had chronic recurrent pleurisy for four years, the last attacks becoming more acute and finally showing what appeared on x-ray examination to be collapse of the left lower lobe. In the differential diagnosis the following factors should be considered: the initial history of trauma, the question of whether there was an underlying tumor, and the possibility that the whole picture could be explained on the basis of chronic infection. Before the implication in the record that all the difficulty was pleural is accepted too readily and since x-ray study was reported as showing the disease to be in the lower lobe, it would be well to see the films — lesions below the diaphragm, causing elevation of the diaphragm and partial compression of the lung, are often misleading. A herniation through the diaphragm may cause obstruction to major bronchi.

DR. MILFORD D. SCHULZ. The films of the chest show an area of increased density occupying the position of the left lower lobe, which seems to be reduced in size. The gas bubble of the stomach rides higher than usual. The left leaf of the diaphragm is not visible, but because of the position of the gas bubble in the stomach I am certain that it is elevated.

DR. DAVENPORT. Are you also certain that there is no evagination of the diaphragm, with abdominal organs in the chest?

DR. SCHULZ. There is nothing to make one think of such a condition. The right lung and the chest elsewhere appear normal. I do not see the tuberculosis that was reported to have been found elsewhere in the chest.

DR. DAVENPORT. On the basis of the symptomatology, which includes no gastrointestinal disturbance in this period of four years and on the basis of the x-ray films, the premise that the lesion was actually above the diaphragm can be accepted. I believe that one can go farther on the basis of this film and rule out any mechanical obstruction due to such a lesion as aneurysm of the aorta, which can block the lower lobe and cause confusing symptomatology. Hilar lymph nodes large enough to cause such obstruction are usually of sufficient size to cause some suspicion in the x-ray films.

Taking all these points in chronologic order in attempting to arrive at a final diagnosis, one should evaluate the onset of the illness and determine whether the abrupt onset four years previously was traumatic enough to explain the whole picture. The presenting symptom when the patient first consulted a physician — the sudden onset of left-sided chest pain while he was at work — suggests the possibility of spontaneous pneumothorax. X-ray films taken at that time, however, failed to disclose any air within the chest and showed only a thickened pleura. The subsequent course, with repeated attacks becoming progressively severer and finally accompanied by infection, is not the picture that is seen with spontaneous pneumothorax. I believe that the persistence of thickened pleura over a period of years means the persistence of some type of infection. A thick pleura is often seen on x-ray examination, particularly in cases of long-standing infection in which the infection, whether pyogenic or tuberculous, finally subsides and the shadow that is called thickened pleura in the x-ray film also clears. The trauma that called the patient's attention to some pre-existing disease four years previously is rather difficult to evaluate, but I believe that trauma can be dismissed as being responsible for the subsequent events.

The question of both benign and malignant tumor must be considered. Some of the most puzzling cases have occurred when the primary difficulty was benign. Adenomas cause bronchial blockage, with suppuration behind such a block. The rule in this type of case, however, is that such patients present evidence of infection, with block behind the tumor mass and subsequent extension of the suppuration into the pleura, so that such a presenting symptom as pleurisy is not usually the initial complaint. Such a possibility, of course, cannot be clearly excluded on the basis of the information that is given in the record, but for the moment will be regarded as unlikely.

So far as malignant tumors are concerned, one is also faced with the four-year history, as well as symptoms that, according to the record, quite clearly began with pleurisy. This raises the question of a pleural endotheoma, a type of cancer that is not accepted as being a frequent neoplasm in the chest. The general opinion is that most cases showing pleural invasion at autopsy have cancer in the bronchus as the original focus. Such cases are reported but are rare in our experience, and a four-year history of a wildly growing pleural endotheoma is most unusual. Malignant tumor of the bronchus must be considered, but is unlikely in view of the fact that the symptoms began four years previously. The periods of as long as a year between attacks are unusual with malignant tumor. The onset and the lack of evidence of suppuration are against the possibility that the initial process was

become eligible for election as president-elect, which happened by unanimous vote

The election of Dr. Fouts to become speaker naturally followed in order because he has been assistant speaker for several years at least. He is a very hard, earnest worker and in my memory the first man from the x-ray field to be elected to that position. The election of Francis F. Borzell, of Philadelphia, to be vice-speaker was an excellent choice. He is another hard working, entirely co-operative man.

Many spoke of the work of James McCann, of Massachusetts, in connection with his work on the principles of the Blue Shield. We are also fortunate, I think, in Joseph Lawrence, who serves as a very good sounding post for the American Medical Association in Washington.

The 1946 meeting will be held in San Francisco from July 1 to 5, the delegates from California spoke of their plans and hopes and felt certain that by that time transportation difficulties would be largely a matter of history, emphasizing the availability of hotels to take care of the number probably coming. The meeting in 1947 is to be held in Atlantic City, and that in 1948 in St. Louis.

The meeting dissolved after three very strenuous days and with a feeling, as I have said above, that almost too much was attempted. But the reason for the attempt I have also stated — the element of uncertainty in Washington.

DAVID D. SCANNELL

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 32371

PRESENTATION OF CASE

A twenty-four-year-old farmer entered the hospital because of attacks of pleuritic pain.

Four years before admission, while lifting packing cases, the patient had a sudden knifelike pain in the left chest, in the region of the axilla. It was made worse on deep inspiration and on change of position. A physician took x-ray films, which were interpreted as showing pleurisy. There were no chills, fever, cough or general malaise. The chest was strapped, and the pain subsided completely for a year, when an identical attack occurred while the patient was at work. X-ray studies showed a thickened pleura. Three or four days of strapping again gave complete relief for a year, when a third attack occurred, with a temperature of 104°F, which lasted a few hours. A slight cough accompanied the attack, in the course of which he spat up about 30 cc of bright-red blood. An x-ray film taken at a tuberculosis sanatorium was reported as showing a thickened pleura. The fourth and severest attack occurred five months before admission while the patient was driving a truck. Again the temperature rose to 104°F and subsided within a few hours. There was no cough, sputum or hemoptysis. The pain lasted three or four days. X-ray examination at the sanatorium was said to show two or three "spots" of tuberculosis in the lung. Three additional x-ray films at another sanatorium were reported as showing only a thickened pleura. Four months before admission drench-

ing sweats occurred almost every night for three weeks but did not recur. During this acute episode the patient lost 15 pounds, which he rapidly regained on returning to work. During the three months before admission he felt well for several days at a time and then, particularly in poor weather, felt weak, lost his appetite and was forced to go to bed for a few days. These attacks were not accompanied by pleuritic pain or fever. Because of persistent symptoms he consulted another physician, who after fluoroscopy stated that the left lung was "dead" but that the patient did not have tuberculosis and could be cured in ten weeks. No tuberculin test, sputum examination or chest tap had ever been performed. For a few weeks before admission, while the patient was doing heavy work, dyspnea, accompanied by a slight cough productive of a small amount of yellow sputum, occurred for the first time. There had been no known exposure to tuberculosis.

Physical examination revealed a slightly diminished expansion of the left chest. The percussion note was dull over the entire left chest, with diminished breath sounds and loss of tactile and vocal fremitus. No rales were heard.

The temperature was 100.5°F, the pulse 100, and the respirations 20. The blood pressure was 128 systolic, 86 diastolic.

Examination of the blood showed 12.6 gm of hemoglobin and a white-cell count of 11,500, with 67 per cent neutrophils. The urine was normal. The sedimentation rate was 6 mm in fifteen minutes, 24 mm in thirty minutes, 30 mm in forty-five minutes and 33 mm in sixty minutes.

An x-ray film of the chest showed the diaphragm to be high and fixed on the left side. There was extensive density throughout the lower third of the left lung field. The heart shadow was displaced to the left, and the hilus was displaced downward. In the lateral view the density appeared to represent a collapsed left lower lobe.

Bronchoscopy was performed on the fourth hospital day. The lower lobe bronchus was reddened, containing a moderate amount of thin, bloody secretion and some friable tissue that bled easily and was regarded as being possibly inflammatory. On the posterior wall, however, there was one

proved to be active tuberculosis, that point need not disconcert us too much. It must be realized that there may have been a bronchial tumor, with secondary infection in the bronchus, and that the bronchoscopist at the time of examination may have run into inflammatory tissue above the level of tumor. We are told that a biopsy showed only chronic granulation tissue, and there is no definite evidence of sputum studies. The most probable diagnosis must be chosen on a percentage basis. Tuberculosis, being a frequent type of infection, produces an inflammatory picture similar to that reported in this case. I am well aware that without more evidence and more definite studies than were reported in this case the diagnosis may come as a surprise.

DR EDWARD B. BENEDICT: What was your final diagnosis?

DR DAVENPORT: Tuberculosis.

A PHYSICIAN: Do you consider multiple infarcts a possibility?

DR DAVENPORT: Not a likely possibility, in view of the subsequent episodes that were accompanied by sputum and a high temperature.

DR BENEDICT: I bronchoscoped this patient, and my preliminary diagnosis was adenoma of the bronchus. That was based on the fact that he was a young man with a history of repeated hemoptysis and repeated attacks consistent with intermittent bronchial obstruction. When I looked down the bronchus there was one area that had the smooth, firm appearance that is consistent with adenoma. The biopsy report, however, was chronic inflammation so that we were somewhat puzzled, but Dr. Richard Sweet who did the operation decided that resection was indicated, on the basis of x-ray evidence of a collapsed lobe.

CLINICAL DIAGNOSIS

Adenoma of bronchus

DR DAVENPORT'S DIAGNOSIS

Collapse of left lower lobe, due to bronchial obstruction, presumably tuberculous

ANATOMICAL DIAGNOSES

Adenoma of bronchus

Bronchiectasis

Chronic pneumonitis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN: I am sorry that Dr. Sweet is not here. His preoperative note reads, "This man will not really get well until he has a lobectomy." When lobectomy was performed, a small, shrunken, hard, left lower lobe that was completely atelectatic and moderately adherent all around and to the diaphragm as well was found. When I examined

the lobe in the operating room, there was a good-sized tumor in the main left lower bronchus. I could not be absolutely sure whether or not the resected edge contained tumor, but a rapid frozen section from the resected edge revealed tumor typical of a benign adenoma. Dr. Sweet, therefore, took out the upper lobe because the tumor would undoubtedly continue to grow in the bronchial stump that still remained. He had originally resected as much of the lower-lobe bronchus as he could without sacrificing the upper lobe.

When the specimen was examined later there was complete occlusion of the dorsal division bronchus leading to the apex of the lower lobe. About half the tumor was extrinsic to the original tumor in the dorsal branch, the other half having extended through into the posterolateral division bronchus, which was almost completely occluded. The tumor measured 2 cm in its greatest diameter. There were numerous enlarged inflammatory lymph nodes all around this bronchus and all along the trachea. A section through the lung parenchyma itself showed extensive bronchiectasis and pneumonitis.

DR BENEDICT: This is an example of what Dr. Davenport meant when he said that one sometimes finds a great deal of inflammatory tissue around the tumor and that a biopsy is often not diagnostic.

DR ALLAN M. BUTLER: I think that this case is also a good illustration of the importance for a surgeon to decide not to obtain further information but to operate, because operation was indicated no matter what the diagnosis was.

DR CASTLEMAN: The patient had, as the physician said, "a dead lung."

DR ALLEN G. BRAILEY: What was the cause of the pleurisy?

DR CASTLEMAN: Bronchial obstruction produced pneumonitis, followed by pleurisy.

CASE 32372

PRESENTATION OF CASE

A nineteen-year-old unmarried woman entered the hospital because of pain in the lower abdomen.

The patient was apparently well until eight hours before admission, when she awoke with a feeling of indigestion and epigastric discomfort. Shortly thereafter the discomfort shifted downward, and she began to have increasingly severe lower abdominal pain. She also became nauseated and vomited everything eaten. A physician sent her to the hospital after administering morphine and atropin.

The patient began menstruating five years before entry, and the periods had always been normal and regular. The last menstrual period, which had begun two days before entry, was in no way unusual. She persistently denied sexual intercourse or having missed any recent period. She had had

due to a plugging of a bronchus by either a benign or malignant tumor

If one gives little weight to the onset of the symptoms on a traumatic basis and further to the possibility of a benign or malignant tumor, a third possibility remains — namely, infection, which would have to be extremely chronic to last four years and explain the whole picture. The ordinary pyogenic infections can probably be excluded, and yet such infections are often present for a number of years. In such cases the diagnosis is obscure, but the presenting symptoms and subsequent course move more swiftly than those in the case under discussion. So far as infection is concerned, infectious granulomas, such as syphilis, tuberculosis and the obscurer types of fungous infection should be considered. Syphilis of the lung, if one excludes congenital syphilis, is an extreme rarity, and I use that redundancy deliberately. It is consequently rather difficult to tie up any of the symptoms with even the types of syphilis of the lung that are reported in the literature, and such a diagnosis can probably be dismissed.

The infectious granulomas of the fungous type can be confined to actinomycosis, because actinomycosis in this part of the country is the most frequent of the fungous infections and the one that has given the obscurest forms of pulmonary disease for long periods of time. The only clue in the history is the fact that this patient was a farmer, and actinomycosis occurs oftener among the rural than among the urban population. Cases among city workers have recently been seen in this hospital, however. I recall a stenographer some years ago who to the best of her recollection had not even spent her vacation in the country. She had a long history, with x-ray changes suggestive of tuberculosis for a period of years, and not until the chest was opened was the diagnosis of actinomycosis made. There are several points to remember in considering such a possibility. The sulfur granules show up only in accumulations of pus, and it has been our experience that the fungus in the sputum is extraordinarily difficult to identify. There are several considerations against accepting this as a likely diagnosis. First, it is relatively rare in spite of the fact that it is one of the types frequently encountered. Secondly, actinomycosis of any appreciable duration almost always causes draining sinuses in the chest, although cases have been reported in which actinomycosis has been a factor during a period of years without causing the typical draining sinus that is usually associated with this type of disease. A primary pulmonary form of the disease, with secondary pleural involvement, occurs, and most of these cases show hemoptysis, which was noted in the case under discussion.

The laboratory data are meager, and I take it that the statement that there were no examinations

of the sputum and no tuberculin test or chest tap is true, and that no bronchoscopic aspiration was performed.

DR. BENJAMIN CASTLEMAN That is correct.

DR. DAVENPORT We then come to the last and I believe the most difficult diagnosis to consider seriously, accepting the fact that we have a rather obscure history and rather less than the usual data that are furnished in such a case. We do not have a negative blood Wassermann or Hinton test to lean on. Because of the greater incidence of tuberculosis in the population, an atypical form of tuberculosis causing this symptomatology is much more frequent on a percentage basis than a typical form of an obscure type of condition. This is the possibility to which most weight should be given. If the onset four years previously is accepted as being due to infection of the pleura, the recurrent pleurisy is quite consistent with tuberculosis, causing fibrinous and later fibrous adhesions with elevation of the diaphragm. Uncomplicated tuberculous pleural effusion is probably never seen. Most authors believe that even a primary pleural effusion not complicated by parenchymal aspects, as in the case under discussion, is due to some underlying focus of disease in the lung, whether or not demonstrated in the x-ray film. In this case, after four years of repeated attacks of pleurisy, there was increasing evidence of involvement of the left lower lobe, which can be explained on the basis of involvement of the bronchial mucosa by tuberculosis. This condition has become more and more appreciated in the last few years, since it has been looked for and since repeated bronchoscopic examination has been performed. It accounts for the previously obscure localization of active tuberculous disease in the bases, as well as for the fibrotic stenoses with partial obstruction, atelectasis and poorly aerated lower lobes that are the end result of a fibrostenosis due to tuberculosis. The one thing that worries me about the diagnosis of tuberculous pleurisy in addition to associated bronchial tuberculosis is that in my experience such patients have a distressing, continuous cough. In this case, as the record points out, there were long periods during which the patient was free from all pulmonary symptoms. In such a situation sputum is often difficult to obtain, and if the disease is active in the bronchial mucosa there is a certain amount of blockage of the parenchymal disease and the patient may go for a long time without the demonstration of tubercle bacilli on sputum examination. It is somewhat unlikely that the patient was studied in this hospital and in the sanatorium without more emphasis on the sputum examination. I rather expect that if the complete history were known there would be disconcerting evidence that previous sputum examinations performed elsewhere were negative. Since negative examinations have been reported in cases that subsequently

ANATOMICAL DIAGNOSIS

Double intussusception and volvulus of ileum, led by adenomatous polyp.

PATHOLOGICAL DISCUSSION

DR. HERRERA At operation the cystic mass was found to be bowel, with a double intussusception, which in addition had rotated on the mesentery so that the intussusception below it had also formed a volvulus. It was impossible to reduce the intussusception, and since the bowel was obviously gangrenous, resection was carried out with a side-to-side anastomosis.

DR. CASTLEMAN The specimen we received in the laboratory consisted of a double ileoileal

intussusception. We were also unable to reduce the intussusception because of the extensive gangrene and interadherence. By cutting across the bowel, we unraveled the different layers and found that the mass that led the intussusception was an adenomatous polyp, which was almost completely infarcted. The first intussusception, which was about 25 cm in length, in turn had intussuscepted for a distance of 30 cm, so that 60 cm of small bowel was involved in a double intussusception. I believe that this was the youngest patient in the adult series that we have seen. When the condition occurs in children, it is usually not due to tumor.

a slight intermenstrual discharge. The appetite had been good, although she suffered from occasional constipation or transient indigestion. She had had a normal bowel movement on the day of entry. There had been no urinary symptoms.

Physical examination revealed the heart and lungs to be normal, except for a soft systolic murmur, varying somewhat with respiration and heard over the entire precordium, although it was loudest at the apex. The abdomen was soft, and a smooth, firm, slightly tender lower abdominal mass could be felt in the midline, reaching up to the umbilicus. Peristalsis appeared normal although somewhat sluggish. Pelvic examination revealed a narrow introitus, which seemed to be virginal. The cervix was normal to palpation, and no pain was elicited by motion. The fundus was small and could be felt separate from and anterior to the abdominal mass, which had pushed it somewhat to the left. There was some tenderness high in the left vault. The patient was menstruating.

The temperature was 99.4°F, the pulse 100, and the respirations 24. The blood pressure was 130 systolic, 70 diastolic.

Examination of the blood revealed a hemoglobin of 12 gm and a white-cell count of 18,000, with 86 per cent neutrophils. The urine was normal.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR GORDON A. DONALDSON. The diagnosis in this case is either quite obvious or extremely obscure, and in keeping with the usual outcome of cases discussed at these exercises I suspect that we had better stick to the most obvious. Certainly the resident in the Emergency Ward who saw this patient believed that the diagnosis was obvious because the studies obtained were minimal. I take it that no x-ray films were made.

Without laboring too many other possible diagnoses, there are one or two features that are worthy of comment. In the first place, if one were looking for a more typical story for an acute inflammation of the appendix, it would be difficult to find even in Zachary Cope's description of typical acute appendicitis. In this case there is the classic type of pain, with the typical shift downward, consistent with the history of eight hours' duration. The nausea and vomiting, which I suspect occurred after the pain, classically in acute appendicitis often precede the pain. This is a minor point, however, the difference probably depending on whether the appendix is mechanically obstructed or diffusely inflamed. A diagnosis of acute appendicitis with appendiceal abscess formation cannot be made, in view of the pelvic and lower abdominal findings. An appendiceal abscess is not likely to reach such proportions in such a short time.

With this history of intestinal obstruction, probably reflex epigastric discomfort and radiation of

pain down into the seat of the disease, one must also think of diseases along the course of the terminal ileum. Could there have been a lesion in a Meckel's diverticulum—perhaps a foreign body? We have recently seen a patient with a huge gallstone in a Meckel's diverticulum that finally led to ulceration and abscess formation. Tumors in this region and intussusception are all inconsistent with the large pelvic and lower abdominal mass. Presumably, this patient had had rheumatic fever, but I cannot tie in such a mass with a diagnosis of rheumatic fever in a patient who eight hours previously had been well. I do not like the reference to the possibility that she was pregnant, I consider the story and physical findings inconsistent with extrauterine pregnancy.

Other possibilities in the region of the pelvis come to mind: hematosalpinx in one tube, presumably the right (but I think that is unlikely), and torsion of a pedunculated fibroid, which had grown during the course of menstrual life. If this was a fibroid it was certainly of tremendous size, and one that is not seen in a patient of this age.

Throughout the physical examination attention is focused on the lower abdominal mass, which evidently lay posterior to the fundus of the uterus, displacing it anteriorly and slightly to the left. It was of such size and weight that it was probably responsible for the pelvic congestion and intermenstrual discharge. This tumor, moreover, had undergone a recent inflammatory change, probably the result of torsion, which accounts for the elevation of the white-cell count and temperature, and was tender to palpation. The most obvious organ involved and the one responsible for this patient's symptoms was the ovary, probably the right ovary, and in a patient of this age the likeliest diagnosis is dermoid cyst.

DR BENJAMIN CASTLEMAN. A cyst that had twisted?

DR DONALDSON. Yes.

DR RODOLFO E. HERRERA. When we saw this patient we also could not help being impressed by the mass in the abdomen, and that was the reason for the lack of additional laboratory and x-ray studies. The mass was easily palpated on abdominal examination, and our preoperative diagnosis was the same as Dr Donaldson's. We examined the pelvis and rectum, both with and without anesthesia, and the only thing that was disturbing about the diagnosis of ovarian cyst was that the mass could not be felt well from below and did not seem to rise from the pelvis. We explained the difficulty simply by saying that it had a long pedicle that had twisted.

CLINICAL DIAGNOSIS

Twisted ovarian cyst.

DR DONALDSON'S DIAGNOSIS

Twisted ovarian dermoid cyst.

the care of the sick has not been made available obviously it is highly desirable to train a certain number of graduate nurses who have had a broad educational background so that they can fill teaching, administrative and supervisory positions. On the other hand, the chief function of a nurse is the bedside care of the patient — a duty that some of the graduates of the modern school of nursing appear path to assume.

The editorial states that the Virginia Board of Nurse Examiners should seek a solution without being influenced too much by sources that insist that most schools should turn out a type of graduate who is able to pass the board examinations of any or all states. It suggests that the Virginia schools immediately convert to a two-year course, with a substantial reduction of the didactic work, and that the large schools, particularly those in teaching centers, should be encouraged to offer postgraduate courses in specialized training for a certain number of these two-year graduates. Undoubtedly two years is an adequate period to train a person in bedside nursing. But, the editorial points out, one of the major objections made by nursing educators is that a two-year graduate is not recognized by the boards of nursing in many states. The answer is simple. If a two-year graduate so desires and has the necessary aptitude, she may continue her education for one or more years and thus become eligible to take the board examinations in the thirty-eight states that now require three years of training, as well as qualify for a teaching, administrative or supervisory position. The advantages of this scheme, as stated in the editorial, are as follows: the shortening of the period of training and the reduction of expense to the pupil would attract larger numbers, one class of nurse of high quality would be continued, better specialists would result from the planned postgraduate courses, and the care of the sick would be restored as the primary duty of the graduate nurse. This seems to be a logical approach to the problem.

The two-year graduate should not be considered as a substitute for the so-called "attendant nurse." The latter should be encouraged but never with the idea of having her take the place of an adequately trained young woman with at least a high-

school education. The attendant nurse has a definite place, particularly in the home, but should not assume those responsibilities in bedside nursing for which she is unqualified by educational background and training. She and the registered nurse with the proposed two-year course of training should be complementary to each other.

By such measures, any state, especially those with a large number of small hospital training schools, should be able to provide enough young women adequately trained in clinical nursing to care for the sick in hospitals and homes. This two-year type of trained nurse does not need (nor would many desire) to be registered in all states. There would however be ample opportunities to provide further educational background for those who are able, willing and suitable for supervisory positions in hospitals, large or small. The trained attendant would take over from both classes of trained nurse many of the routine duties that are time consuming and the performance of which does not require a high-school education — let alone two or more years in a training school for registered nurses. A certain number of two-year graduates, by virtue of postgraduate study, and possibly of advanced preliminary education, would be qualified to assume highly responsible positions. The majority would be capable of rendering excellent bedside care, although they would not be permitted, under existing statutes, to take board examinations in many other states. Finally, the attendant nurse would assume many of the time-consuming routine duties that do not require skilled service.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CROSBIE — Arthur H. Crosbie, M.D., of Boston, died August 23. He was in his sixty-ninth year.

Dr. Crosbie received his degree from Harvard Medical School in 1903. He was a consulting urologist at the Massachusetts Women's Hospital, Boston, and St. Elizabeth's Hospital, Brighton, and surgeon-in-chief, Department of Urology, Cambridge City Hospital, Cambridge. His memberships included the New England Surgical Society, American Association of Genito-Urinary Surgeons, American Urological Association and American College of Surgeons.

His mother and five brothers survive.

SARGENT — Ara N. Sargent, M.D., of Salem, died August 26. He was in his seventy-ninth year.

Dr. Sargent received his degree from Harvard Medical School in 1893. He was a member of the American College of Physicians and a fellow of the American Medical Association.

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NEW ENGLAND POSTGRADUATE ASSEMBLY

THE program of the fifth New England Postgraduate Assembly, which will be held on October 30 and 31, appears elsewhere in this issue of the *Journal*. These meetings were inaugurated in 1938, were held through the following three years but were canceled during the war years. Some idea of their popularity and their value as one means of postgraduate medical education may be gained from the fact that in one year the total registration was 925.

As in the past, the Program Committee has arranged for a series of talks by eminent physicians who, by and large, are not residents of New England.

The choice of topics has been excellent and has resulted in a program that should prove to be of interest to all practicing physicians.

There are two innovations. In the first place, the meetings will be held in downtown Boston, — at the Hotel Bradford, — which should appeal to those who plan to stay in Boston during that time. Secondly, there will be a technical exhibit by a number of commercial firms, which should offer an excellent opportunity for all registrants to become acquainted with recently introduced drugs, the latest type of instruments and other material currently available to practicing physicians.

The facts that the majority of medical officers have been discharged from active duty and that civilian physicians have been relieved of a great deal of the pressure under which they worked during the war years should result in a record breaking attendance. It would be difficult to devise a two-day program that would offer more in the way of a means of becoming acquainted with recent advances in diagnosis and treatment.

SHORTAGE OF NURSES

MUCH has appeared recently in the lay press regarding the critical situation created by the shortage of nurses, and the *Journal* commented on it editorially in the July 11 issue. Many reasons have been advanced for the present crisis, but little has been done to remedy it. An editorial, entitled "The Training of the Graduate Nurse," in the July issue of the *Virginia Medical Monthly* suggests an underlying cause that has been present for many years and offers suggestions for its correction.

This editorial maintains that recent trends in nursing education have been largely responsible for the present situation. It is certainly well recognized that, at least in Massachusetts and probably in other states, many of the small nursing schools have been forced to close because they could not meet the increasing educational requirements for the registration of their graduates. In other words, in the attempt to raise the standard of nurses a sufficient proportion of persons who are willing to

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TWELVE YEARS' EXPERIENCE IN ROENTGENOTHERAPY FOR CHRONIC ARTHRITIS*

JOHN G. KUHN, M.D.,† AND SIDNEY L. MORRISON, M.D.‡

BOSTON

ROENTGENOTHERAPY as a local treatment to the joints in chronic arthritis was begun by us over twelve years ago. We were prompted to institute this form of treatment after reading the early optimistic reports of Kahlmeter¹ in Sweden and of Scott² in London. At first the treatments were given with great caution. After a number of unexpected successes and an equal number of failures, a general plan of treatment for certain articular lesions in chronic arthritis was developed. During this time we learned to expect certain effects in the joints, and by trial and error we found some of the indications and contraindications to the treatment. By the end of August, 1945, x-ray therapy had been given to 370 selected patients, of whom 252 had rheumatoid arthritis and 118 osteoarthritis. Five hundred and sixteen separate joints were treated, exclusive of spines. In the majority of cases one joint was treated. Although a large number of patients were treated for various types of nonarticular rheumatic disease, such as fibrositis and bursitis, these have not been included in this study.

The articular lesions of chronic arthritis have been treated with x-ray almost from the time of Roentgen's discovery in 1896. In 1897 Sokolow³ published the first report on this treatment, claiming that it gave relief in arthritis deformans. The first American report was made in 1906 by Anders, Daland and Pfahler.⁴ Since the beginning of the century numerous studies have appeared and, almost without exception, have claimed improvement in chronic arthritis following roentgenotherapy. Staunig⁵ reported in 1925 that he had treated 400 patients. In 1933 Langer,⁶ stating that therapy had been beneficial in 200 cases, advocated x-ray treatment to the spinal ganglions, since he believed that one of the main actions was on the sympathetic nervous system. By 1935 2000 arthritic patients had been treated by von

Pannevitz,⁷ who reported improvement in more than 95 per cent. Between 1925 and 1937 Kahlmeter⁸ treated over 5000 patients, although excellent results were claimed; in the entire group, he stated that the best results were seen in the early stages of arthritis. Scott,⁹ who was one of the pioneers in roentgenotherapy for arthritis, in 1939 advocated wide-field x-ray therapy, which he reported to be particularly valuable in rheumatoid arthritis of the spine.

The first carefully controlled study on the effect of roentgenotherapy in chronic arthritis was made in 1941 by Smyth, Freyberg and Peck¹⁰ on 100 unselected patients with various forms of rheumatic disease. They concluded that significant improvement that could be attributed to the therapy occurred in only 14 per cent of patients. Definite relief, however, followed roentgenotherapy in 72 per cent of patients with rheumatoid arthritis of the spine. They believed that much of the improvement reported by earlier writers was largely subjective. In the earlier papers little in the way of statistics or objective data was given. The findings were difficult to evaluate because of confusion of local with systemic changes and of subjective with objective improvement. The suggestive effect of this form of therapy on certain patients is often profound. For this reason subjective impressions must always be viewed with suspicion. The x-rays undoubtedly exert some systemic effect, but such systemic changes are inconstant and usually immeasurable. These varied reports on the value of roentgenotherapy led us to analyze our objective and measurable findings in the treatment of a selected group of patients suffering from chronic arthritis.

METHOD OF TREATMENT

Our technic of treatment was similar to that reported from both European and American clinics. The method varied in different joints, depending on the tissues to be penetrated and on the anatomic area to be covered. As a rule 200 r was given twice a week over two to four target areas for six treat-

*Read at a meeting of the Boston Orthopaedic Club, Boston, December 19, 1945.

From the Robert Breck Brigham Hospital.

†Assistant in orthopedic surgery, Harvard Medical School, chief of surgical and orthopedic staffs, Robert Breck Brigham Hospital.

‡Roentgenologist, Robert Breck Brigham Hospital.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

POSTPONEMENT OF SCHOOL OPENING INADVISABLE

Every year the question comes up Should school opening be delayed because of the incidence of poliomyelitis in the town or in neighboring towns? The Department of Public Health strongly urges that the schools be opened at the usual time and be kept open

There is nothing to be gained by keeping the schools closed Experience shows that spread of the disease is not prevented by any such measure On the other hand, by keeping the schools open the child is under the observation of school physician, nurse and teacher in addition to that of the parents at home In this way the early stages of infection are likelier to be detected, the child being isolated and brought under proper medical supervision Missed cases too frequently result from the unsupervised mingling of children when schools are not in session

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender Books that appear to be of particular interest will be reviewed as space permits Additional information in regard to all listed books will be gladly furnished on request

A Synopsis of Medicine By Sir Henry L Tidy, K B E, M A, M D, B Ch (Oxon), F R C P (Lond), consulting physician to St Thomas's Hospital, London Eighth edition, revised and enlarged 12°, cloth, 1215 pp Baltimore Williams and Wilkins Company, 1945 \$7 50

This standard compendium, first published in 1920, has been thoroughly revised and brought up to date, especially in the field of therapeutics The use of the sulfonamides has been incorporated into the sections on infectious diseases, and the chapter on the hemolytic anemias of the newborn has been rewritten in relation to the Rh factor Many new disease syndromes have been included, and the discussion of other diseases has been amplified Vitamin K is included for the first time, and there is a new article on sex hormones Many articles have been extensively rewritten, resulting in an addition of about forty pages to the text The work is well arranged and, although based on British practice, should prove useful to the practicing physician as a ready source of reference

Lights Out By Baynard Kendrick 8°, cloth, 240 pp New York William Morrow and Company, 1945 \$2 50

This is the story of a blinded soldier and his conditioning in Army hospitals for a normal everyday life

NOTICES

ANNOUNCEMENT

Dr Lendon Snedeker announces his return to the practice of pediatrics at 319 Longwood Avenue, Boston

METROPOLITAN STATE HOSPITAL

The twelfth Postgraduate Seminar in Neurology and Psychiatry will begin Friday, October 11 The program will be as follows A review course in basic neurology and psychiatry, consisting of eighty-one lectures, to be held every Friday from 2:00 to 10:00 p m from October 11 to December 13, 1946, and from January 3 to April 25, 1947, at the Metropolitan State Hospital, 475 Trapelo Road, Waltham, a course in social and special psychiatry, consisting of thirty-six lectures, to be held every Wednesday from 5:30 to 10:00 p m from October 16 to December 11, 1946, and from March 19 to May 14, 1947, at the Boston Psychopathic Hospital, 74 Fenwood Road, Boston, and a course in pediatric neuropsychiatry (child psychiatry), consisting of twenty lectures, to be held every alternate Monday from 5:30 to 10:00 p m from October 14 to December 9, 1946, and from March 17 to May 12, 1947, at the Walter E Fernald State School, Waverley

The seminar is open to all graduate physicians, but the number of vacancies for demonstrations in the review course in basic neurology and psychiatry will be limited to twenty-five in each of the subjects of the course neuroanatomy, neuropathology and neuro-röntgenology Those interested are requested to apply in writing before October 7 to Dr William C Gaebler, superintendent, Massachusetts State Hospital, Waltham

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, SEPTEMBER 19

- FRIDAY, SEPTEMBER 20**
*10:00 a m-12:00 m Medical Staff Rounds, Peter Bent Brigham Hospital
- TUESDAY, SEPTEMBER 24**
12:00 m-1:00 p m Dermatological Service, Grand Rounds, Amphitheater, Dowling Building, Boston City Hospital
*12:15-1:15 p m Clinico-röntgenological Conference, Peter Bent Brigham Hospital
- WEDNESDAY, SEPTEMBER 25**
*10:30-11:30 a m Medical Clinic Isolation Building Amphitheater Children's Hospital
*12:00 m Clinicopathological Conference (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital
*2:30-4:00 p m Combined Clinic by the Medical Surgical and Orthopedic Services Amphitheater, Children's Hospital
- *Open to the medical profession

- MARCH 15-SEPTEMBER 15** Boston University Course for Discharged Medical Officers Page 240 issue of February 14
- SEPTEMBER 16-18** American Diabetes Association Page 284, issue of August 22
- SEPTEMBER 23** Diabetes Clinic Page 314 issue of August 29
- SEPTEMBER 30-OCTOBER 2** Congress on Industrial Health. Page 284 issue of August 22
- OCTOBER 6-12** Interamerican Congress of Cardiology Page xix, issue of June 6
- OCTOBER 7-12** Seminar in Legal Medicine Page 206, issue of August 8
- OCTOBER 7-18** New York Academy of Medicine. Page 544 issue of April 18
- OCTOBER 9-11** Association for Military Surgeons Page 346, issue of September 5
- OCTOBER 10** The Present Status of Sympathectomy in Hypertension Dr Reginald Smithwick Pentucket Association of Physicians Page 238, Haverhill
- OCTOBER 11-MAY 14** Metropolitan State Hospital Notice above
- DECEMBER 5** Suffolk Censors' Meeting Page 346 issue of September 5
- FEBRUARY 7** American Board of Obstetrics and Gynecology Page 238, issue of August 15
- APRIL 28-MAY 2** American College of Physicians Page 206 issue of August 8

DISTRICT MEDICAL SOCIETIES

PLYMOUTH

- OCTOBER** Jordan Hospital, Plymouth
NOVEMBER Plymouth County Hospital South Hanson
JANUARY Brockton Hospital Brockton
FEBRUARY Moore Hospital Brockton
MARCH Goddard Hospital Brockton
APRIL State Farm Bridgewater
MAY Lakeville Sanatorium, Lakeville

SUFFOLK

- December 5** Censors' Meeting Page 346 issue of September 5

ent), moderate in 61 (39.9 per cent) and marked in 35 (22.7 per cent). Only 7 patients had complete subsidence of symptoms. The poorest results were obtained in osteoarthritis, but with a selection of the type of joint suitable for roentgenotherapy a fair response was obtained. The improvement occurring in 72.0 per cent of the 118 patients was slight in 29 (24.5 per cent), moderate in 40 (34.0

knee only in 10 patients with practically equal involvement of both knees. The x-ray apparatus and the draping were so arranged that the patients thought that both knees were being treated. The results of these treatments are given in Table 3. Only 1 patient reported that both knees felt better after the treatments, and no objective changes were found in any of the untreated knees. Definite ob-

TABLE 2 *Effects of Roentgenotherapy in Different Types of Arthritis*

DIAGNOSIS	TOTAL NO OF CASES	NO CHANGE		SLIGHT IMPROVEMENT		MODERATE IMPROVEMENT		MARKED IMPROVEMENT	
		NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE
Rheumatoid arthritis without spondylitis	154	32	20.8	26	16.8	61	39.9	35	22.7
Rheumatoid arthritis of spine	98	15	15.4	34	34.7	37	37.7	12	12.2
Osteoarthritis	118	33	28.0	29	24.5	40	34.0	16	13.5

per cent) and marked in 16 (13.5 per cent). In 6 cases there was complete disappearance of symptoms. There were failures in 33 patients, most of whom had deformities of varying degree, as well as extensive spur formation. Mechanical disalignment, which seems to be more significant in osteoarthritis than in rheumatoid arthritis, continues to produce inflammatory changes in the joint, and little can be expected from local therapy until such disalignment has been at least partially corrected.

The selection of articular lesions for roentgenotherapy comprised about 1 in 12 of the patients receiving treatment on the wards. X-ray treatment was regarded not as a cure for arthritis, but as a helpful local measure in certain cases. The chief indication for roentgenotherapy in rheumatoid arthritis was chronic swelling in a joint that failed to subside after several weeks' rest and physiotherapy. Most of these joints respond to roentgenotherapy if there is no serious deformity or internal derangement. Persistent stiffness and pain were the indications in osteoarthritis, in which decrease in swelling is often difficult to measure and the effect of x-ray therapy seems to be chiefly one of analgesia with an increased range of motion at the joint. In rheumatoid arthritis of the spine, a decreased range of chest expansion and severe muscular spasm, with marked forward bowing of the spine, responded fairly readily to x-ray treatment and permitted earlier and more rapid application of corrective apparatus. Roentgenotherapy after manipulative procedures, which was given only during the last year of the study, seemed to lessen muscular spasm and to prevent the reformation of adhesions, but its action was observed for too short a time to justify a definite statement. None of the cases in which such therapy was used after manipulation were included in this study.

To determine the effect of suggestion on the changes observed, the treatments were given to one

jective improvement was observed in the treated knees in 7 cases. In 3 patients with severe deformity there were no objective changes, and only questionable subjective changes in 1. The psychic effect of roentgenotherapy in such patients therefore does not appear to have been an important factor in the improvement.

Kahlmeter⁵ stated that better results were obtained with roentgenotherapy in the early than in other stages of chronic arthritis. A graph was made

TABLE 3 *The Subjective Effect of Roentgenotherapy*

SEX	AGE	TREATED KNEE		UNTREATED KNEE	
		OBJECTIVE IMPROVEMENT	SUBJECTIVE IMPROVEMENT	OBJECTIVE IMPROVEMENT	SUBJECTIVE IMPROVEMENT
F	18	++	++	0	0
M	22	++	++	0	0
M	26	++	++	0	0
F	42	0	0	0	0
F	43	0	0	0	0
F	43	0	0	0	0
F	48	++	++	0	0
F	49	++	+++	0	++
F	53	+	++	0	0
F	56	+	+	0	0

of all patients suffering from rheumatoid arthritis (Fig 1). Although there is a slight decline of the curve with longer duration of symptoms, the variation from year to year is not great. It is probable that the decrease in improvement was due more to the greater number of severe deformities than to the duration of symptoms per se. With a local treatment like roentgenotherapy the condition of the joint at the time of treatment appeared to be the important factor. A comparison of the different types of chronic arthritis showed no significant variation from the graph for cases of rheumatoid arthritis, except that in osteoarthritis the response showed no relation to the duration of symptoms.

ments, 1200 r in six treatments during a period of three weeks comprised a course of treatment, and no further treatments were given to the patient until at least two months had elapsed. In rheumatoid arthritis of the spine, wide-field therapy in doses of 100 r was applied over two spinal areas, an upper and a lower, every other day for twelve treatments, no further therapy was given for two months. The dosage depended on the stage of the disease and the general condition of the patient.

At first an arthritic inflammation that showed little response to rest and physiotherapy was the only indication for roentgenotherapy. Before long,

tion of the forward bowing of the spine were the most important changes observed. Subjective improvement was recorded by questioning the patient about the amount of pain, how freely motions could be performed and how much stiffness was present.

RESULTS

The results of roentgenotherapy in this selected group of patients are shown in Table 1. In most cases the subjective impressions of change were almost parallel to the objective, and although examination failed to verify the improvement claimed by some patients, the number of such cases was

TABLE 1 *Effect of Roentgenotherapy in 370 Selected Patients with Chronic Arthritis*

BASIS	NO CHANGE		SLIGHT IMPROVEMENT		MODERATE IMPROVEMENT		MARKED IMPROVEMENT	
	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE
Subjective impression	69	18.9	94	25.4	163	44.0	44	11.8
Objective impression	80	21.6	89	24.1	138	37.2	63	17.1

however, it was noticed that certain lesions responded fairly readily to x-ray treatment whereas others did not, and roentgenotherapy was therefore prescribed more carefully. The selected group of 370 patients was about one tenth of the total treated on the wards during the twelve-year period.

Since articular changes occur frequently with exacerbations and remissions in the disease, it is essential that patients be observed during a period in which their condition remains relatively unchanged. In such cases x-ray therapy was used as an adjunct to the general medical and orthopedic measures. The patients were compared with an equal number on the wards at the same time who had similar articular lesions whose treatment differed only in the absence of roentgenotherapy. Only changes in the joints that were more rapid and definite in the patients treated with x-ray were recorded as improved, when the changes were no different in the treated and untreated groups the effect of the roentgenotherapy was recorded as negative.

Objective changes were evaluated by observation, by measurement of the circumference of the joint and by recording the range of active, painless motion. If decrease in swelling and tenderness was little, with a decrease in articular circumference of less than 1.3 cm and with an increased range of active, painless motion no greater than 10°, the improvement was recorded as slight. If the decrease shown by articular circumference was from 1.3 to 2.5 cm and there was an increased range of painless, active motion of from 10 to 30°, improvement was recorded as moderate, the effect beyond this was tabulated as marked. Improvement in the spine, although definite, was more difficult to evaluate. Increase in chest expansion and more rapid correc-

relatively small. Of the 290 cases in which objective changes were observed (78.4 per cent of the series) improvement was slight in 89 (24.1 per cent), moderate in 138 (37.2 per cent) and marked in 63 (17.1 per cent). In only 25 of the patients listed as markedly improved, was there complete subsidence of all inflammation and of all symptoms, a rare effect following roentgenotherapy. In 80 patients, or 21.6 per cent, no improvement could be found, this large percentage of failures was probably due chiefly to a faulty selection of articular lesions. Indiscriminate use of roentgenotherapy in all forms of rheumatic disease gave discouraging results, as Smyth, Freyberg and Peck¹⁰ have shown.

There were considerable variations in the effects of therapy in the different types of chronic arthritis (Table 2). The best results were obtained in rheumatoid arthritis of the spine, in which — as pointed out by Scott,⁹ Hare¹¹ and Smyth, Freyberg and Lampe¹² — there is a more rapid subsidence of muscular spasm and pain, an increase in chest expansion and in spinal movement and a decrease or sometimes a complete disappearance of nerve-root pain. Improvement occurred in 84.6 per cent of the 98 patients with rheumatoid arthritis of the spine. Improvement was slight in 34 (34.7 per cent), moderate in 37 (37.7 per cent) and marked in 12 (12.2 per cent). Twelve patients were completely relieved of symptoms, 15 who were not improved showed marked ankyloses and deformities. In most cases, plaster casts were applied and active exercises were given during or soon after roentgenotherapy, usually with continued improvement. There were only 2 relapses. In rheumatoid arthritis without spondylitis, improvement was seen in 79.5 per cent of 154 patients. Improvement was slight in 26 (16.8 per

hours after the first treatment were not unusual. Exacerbation of symptoms after subsequent treatments must be rare, since none were encountered. Among 21 women treated by roentgenotherapy for rheumatoid arthritis of the spine, menorrhea developed in 2, one of whom was twenty-eight and the other thirty-four years of age; the condition persisted in these patients. In a fifty-year-old man a drop in the white-cell count from 500 to 1800 was observed after three x-ray treatments to the spine. The patient complained of pro-

stressed the value of x-ray treatment in limiting and combating acute infections. Ochsner and Mumford,¹⁶ without explaining its *modus operandi*, found that roentgenotherapy was helpful in relieving pain in lesions of the bones and joints. In chronic arthritis following x-ray treatment Hernaman-Johnson¹⁷ observed local analgesia, absorption of articular exudate, decreased thickness of the articular capsule and increased density of the bone.

In recent biopsy studies following roentgenotherapy to the joints of both dogs and patients suf-



FIGURE 2 Roentgenograms before and after Roentgenotherapy in a Fifty-Year-Old Man. The film on the left was taken before treatment. The film on the right, taken six months later, reveals no significant changes, except for a possible slight increase in osseous density.

found weakness, and the leucopenia was an incidental finding. X-ray treatments were discontinued. Three weeks later the white-cell count returned to 7000. In no other case was any change observed in the blood. The sedimentation rate was not altered in any case, and no significant changes in the results of other laboratory tests were recorded.

DISCUSSION

The effect of x-rays on the tissues of the joint is not fully known. It is generally assumed that the action is almost wholly local, in spite of the early uncritical assumption that systemic changes result. Some of the action is probably destructive of newly formed connective tissue, as suggested by Röhr.¹⁸ Ewing¹⁴ enumerated the following chief effects of x-rays on the tissues: destruction of rapidly proliferating cells, increased permeability of the cell membrane, inhibition of cell ferments, vascular changes, and lymphatic exudation. Desjardins¹⁵

suffering from intermittent hydrops, Horwitz and Dillman¹³ found a disappearance of edema from the tissues and a diffuse fibrous thickening of the vascular walls, with obliteration of the lumens of the small vascular channels. In dogs doses up to 8000 r led to loss of fur and slight superficial ulceration of the skin, but no changes in the joints. In studying the effects of x-rays on growing epiphyses, Spangler¹⁹ and later Barr, Lingley and Gall²⁰ observed that severe damage and, at times, complete necrosis of the epiphyseal cartilage followed irradiation. The latter investigators also found that irradiation amounting to 1335 r or more caused epiphyseal damage in rats, but that no changes were found in the joints. Hatcher²¹ reported the development of sarcoma in 3 patients given roentgen or radium irradiation; in a review of the literature he found that extremely large doses had been given whenever this complication occurred.

The patients in this study demonstrated a diminution in swelling, frequently rapid subsidence of articular exudate, extensive local analgesia and a

Since it had been our clinical impression that a greater and more lasting change was ensured if two or more series of treatments were given to the arthritic joints, two or more series were given in 74 patients. A review of the data revealed that if no change was observed with one series little improvement could be anticipated from further x-ray

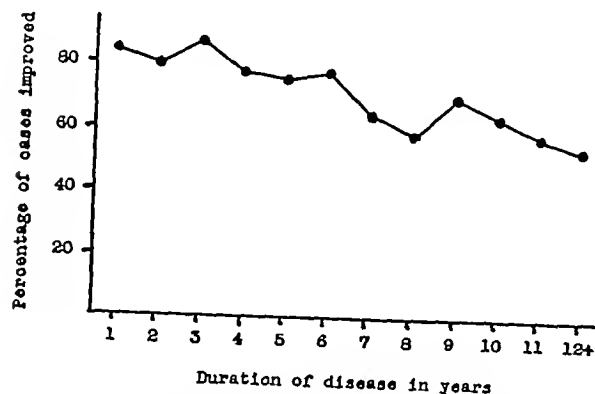


FIGURE 1 *Effect of Roentgenotherapy in Rheumatoid Arthritis in Relation to the Duration of the Disease*

therapy. If a fair amount of improvement occurred from one treatment, slightly more effect followed a second one. The results of one and of two or more treatments are presented in Table 4. A greater improvement was noted in patients receiving two

ment in 18 and with no definite cause in 14, of whom 4 had severe nephritis and 2 severe cardiac disease. The failure of therapy in 15 cases of rheumatoid arthritis of the spine was associated with serious deformity and ankylosis in 7, and no cause could be determined in 8, in which severe nephritis was present in 2.

The majority of these failures, which occurred during the first three years of the study, can be attributed chiefly to a faulty selection of patients. In osteoarthritis with severe articular derangement and spur formation, little improvement can be expected from x-ray treatment. If the deformity is first corrected and the joint made mechanically as efficient as possible, roentgenotherapy hastens subsidence of the inflammation and often removes pain. Metastatic cancer is occasionally found in the presence of chronic arthritis and is often not demonstrable by x-ray for many months. Serious systemic disease and infection should not greatly hinder a local treatment like roentgenotherapy, but the experience in this study suggests that they do. The chief cause of failure, however, was some mechanical disturbance that hindered the subsidence of the articular inflammation. Although x-ray treatment has proved its usefulness in selected cases, the technic has not yet reached the stage at which the results are always predictable. The following conditions are regarded as contraindications to roentgenotherapy: quiescent rheumatoid arthritis without joint inflammation, severe deformity or articular

TABLE 4 *The Effect of the Number of Courses of Treatment in Arthritis*

COURSES OF TREATMENT	NO OF CASES	NO CHANGE		SLIGHT IMPROVEMENT		MODERATE IMPROVEMENT		MARKED IMPROVEMENT		RELAPSES	
		NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE
One	296	70	23.6	69	23.3	109	36.8	48	16.2	17	5.7
Two or more	74	10	13.5	20	27.0	29	39.2	15	20.3	3	4.0

or more series. About the same number of relapses occurred, with recurrence of the inflammatory changes in the treated joint, in both groups. To date repeated courses of treatment cannot be said to guarantee permanency of the changes that take place. Any relapses usually occurred within three to six months after the completion of the series of treatments.

Of the total of 80 cases in which no improvement resulted from roentgenotherapy the failure of treatment was ascribed to the following factors: in 33 cases of osteoarthritis severe deformity or articular derangement in 17, no apparent cause in 9, metastatic cancer (disclosed on subsequent x-ray examination) in 4, active syphilis (found later) in 2, and active tuberculosis (subsequently discovered) in 1. In 32 patients with rheumatoid arthritis without spondylitis, the failure was associated with severe deformity or articular derange-

ment, and serious chronic disease or systemic infection.

Although no serious harm to the patients or damage to the joints was observed with the dosage given, the following reactions occurred: local pigmentation of the skin, 9 cases (2.1 per cent), nausea and vomiting, 8 spinal cases (8.1 per cent), temporary exacerbation of arthritis, 20 cases (5 per cent), amenorrhea, 2 spinal cases (9.5 per cent), and leukopenia, 1 case (0.2 per cent). It was therefore concluded that x-ray treatment must be given with caution. Pigmentation of the skin after roentgenotherapy varied tremendously in different patients, occurring to a marked degree in only 9.

Such pigmentation gradually disappeared after x-ray treatments were discontinued. Nausea and vomiting were frequent after roentgenotherapy to the lower dorsal and lumbar spine. Exacerbation of symptoms in the joint lasting from twelve to twenty-

child in 24.1, moderate in 37.2 and marked in 17.1 per cent

The effect varied in the various types of chronic arthritis. The greatest improvement (84.6 per cent) as seen in rheumatoid arthritis of the spine. In rheumatoid arthritis without spondylitis, 79.2 per cent of patients improved. In osteoarthritis the least improvement occurred — 7.2 per cent.

Suggestion apparently played little part in the results of therapy. The decrease in subjective symptoms almost paralleled the objective changes.

The duration of symptoms had little effect on the end results. The condition of the joint was the most important factor.

Repeated courses of x-ray treatment do not ensure the permanence of the improvement.

Roentgenotherapy is useful in selected cases, and its chief indications are chronic inflammation in a joint that has not responded to rest and physiotherapy, pain and stiffness in osteoarthritis, and muscular spasm and spinal limitation of motion and pain in rheumatoid arthritis of the spine.

In the 80 patients who showed no response to roentgenotherapy the principal reasons for failure were severe deformity or mechanical derangement of the joint, cancer not found in the first x-ray examination and serious systemic disease.

Unpleasant effects, such as a temporary increase in symptoms after the first treatment and nausea and vomiting, were occasionally seen, but no damage to the skin or articular tissues occurred.

Roentgenotherapy should be regarded as a local treatment only — a helpful adjunct to the medical and orthopedic measures that are usually prescribed.

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decrease in muscular spasm followed by an increased range of active, painless motion. In x-ray films taken two months to ten years after roentgenotherapy, no significant changes were observed in the bones. The slight changes in bone density that were found could readily be accounted for by the increased or decreased activity of the patients (Fig 2). X-ray treatment to arthritic joints in 4 children followed four years or more caused no disturbance in growth (Fig 3). No harmful effects on the skin or articular tissues were observed. In

to determine. The local condition of the joint is the chief indication — chronic inflammation or persistent pain and stiffness with no obvious mechanical cause. In rheumatoid arthritis of the spine, with severe bowing of the spine and ankylosis, little improvement follows roentgenotherapy.

X-ray treatment should not be used to the exclusion of other local treatments, but should be considered only a useful adjunct to the usual medical and orthopedic measures. The joints that were not treated with x-ray eventually improved for the most



FIGURE 3 Roentgenograms before and after Roentgenotherapy in a Five-Year-Old Girl. The film on the left, taken before treatment, shows extensive soft-tissue swelling, articular damage, and osteoporosis. That on the right, taken five years later, shows dense bones and no swelling of the soft tissues. Two courses of x-ray treatment had been given. The knee had normal painless motion.

2 patients in whom repeated operations permitted examination of the articular tissues before and after roentgenotherapy no significant changes were seen after a dosage of 1200 r.

The various forms of chronic arthritis are usually regarded as systemic disturbances whose most obvious and severe manifestations are articular lesions. All the evidence at hand suggests that roentgenotherapy is only a local treatment to the affected joints and that its chief use is in patients in whom one or few joints show disability. The spinal joints seem to show the most rapid and definite response to the treatment, which is of little value when severe deformity or articular derangement is present. In such cases the articular inflammation may be caused mechanically by the deformity or the changes within the joint, and it may subside without other treatment when the mechanical disturbance is removed. The seriously ill patient responds slowly to roentgenotherapy — whether this is due to a profound depression of all reparative processes, we are unable

part, but roentgenotherapy hastened the subsidence of symptoms. All that can be expected in selected patients is an acceleration in the process of recovery. The improvement induced by x-rays is not always lasting. 56.2 per cent of patients showed improvement that persisted, without recurrence in the inflammatory process in the joint. We believe that in these cases the natural healing process has continued after improvement was started by the therapy.

The duration of the effect of x-rays apparently varies. In subsequent observation of the 370 patients only 20 showed true relapses, all of which occurred in three to six months after treatment, the average being slightly more than five months.

SUMMARY

In this study of 370 selected patients suffering from chronic arthritis, the improvement that occurred after roentgenotherapy in 78.4 per cent was

The characteristic febrile paroxysms, with associated symptoms and physical findings, occur in delayed primary as well as in recurrent attacks. In Table 1 the incidence of these symptoms and signs is compared in two groups of patients, one of delayed primary attacks and the other of later relapses. Both groups were observed under the same conditions and were treated with the same drug regimens. It is readily apparent that the two groups showed little difference in the incidence of symptoms and physical findings.

Occasionally, however, the recognition of malaria in a delayed primary attack represents a difficult diagnostic problem. In some cases, smears are persistently negative for several days, despite the oc-

currence of febrile paroxysms, with associated symptoms and physical findings, occur in delayed primary as well as in recurrent attacks. In Table 1 the incidence of these symptoms and signs is compared in two groups of patients, one of delayed primary attacks and the other of later relapses. Both groups were observed under the same conditions and were treated with the same drug regimens. It is readily apparent that the two groups showed little difference in the incidence of symptoms and physical findings.

When faced with fever, chills and severe malaise in a patient who exhibits no diagnostic physical findings and has several negative malaria smears, the physician may be tempted to employ sulfonamides or penicillin or to attempt a therapeutic trial with an antimalarial drug. Such temptation should be resisted. Penicillin is of no value in the treatment of malaria, and the sulfonamides and antimalarial drugs can prevent the appearance of malaria parasites and thus make impossible the establishment of a correct diagnosis. It is essential that the diagnosis of malaria be verified by positive blood smears, so that rational treatment can be instituted for the current attack and subsequent attacks can be promptly recognized and properly treated.

TABLE 1 Incidence of Symptoms and Physical Findings in 84 Delayed Primary Attacks and 190 Later Relapses

SYMPTOM OR PHYSICAL FINDING	PERCENTAGE OF DELAYED PRIMARY ATTACKS	PERCENTAGE OF LATER RELAPSES
Chilly sensation	93	95
Chills	93	90
Headache	96	97
Backache	89	93
Generalized aching	91	93
Weakness	96	97
Nausea	52	71
Vomiting	36	49
Dizziness or lightheadedness	27	37
Tinnitus	36	45
Abdominal pain	61	65
Abdominal tenderness	60	65
Palpable spleen	69	71
Palpable liver	52	43
Herpes simplex	27	21

currence of chills and fever and other commonly associated symptoms. Such cases are often differentiated with difficulty from a variety of bacteremias or septicemias. The presence of leukopenia in malaria is of some help in ruling out streptococcal, pneumococcal or staphylococcal bacteremias, but does not differentiate malaria from typhoid fever, dengue or cases of influenza in which respiratory symptoms are minimal.

Some delayed primary attacks are ushered in by an irregular fever, without chills and with negative malaria smears. In some cases the fever eventually assumes a tertian character, providing a clue to the diagnosis, in others a chill occurs after a few days of remittent fever and is followed by a more intermittent febrile course.

The onset of a delayed primary attack may be marked by severe abdominal pain and tenderness, and by nausea and vomiting. When these symptoms occur before a paroxysm supervenes, they simulate closely an acute abdominal condition, but the presence of a low white-cell count is a guide to the correct diagnosis.

All these variants from the typical vivax attack occur in later relapses, as well as in the delayed primary attack. The absence of a previous history of malaria, however, and the greater incidence of nega-

INTERVAL BETWEEN CESSATION OF SUPPRESSIVE MEDICATION AND ONSET OF DELAYED PRIMARY ATTACK

Information on 101 patients with delayed primary attacks was assembled, to calculate the interval between the time of discontinuance of suppressive medication and the date of onset of the first attack. In 96 cases data on the dosage of quinacrine taken for suppression were available. For purposes of analysis, the patients were divided into three groups—those who had taken the usual 0.7 gm of quinacrine during each week, those who had taken more than 0.7 gm per week, and those who had taken less than 0.7 gm per week (Table 2).

It is clear that despite considerable variations in the suppressive regimens used in the endemic areas, the mean interval to onset of the first attack following the end of suppression in each of the three groups was essentially the same—forty-one days. The range of intervals was also similar in each of the groups, and the standard deviation was nearly identical: 23.3 in the first, 22.9 in the second and 21.3 in the third. Accordingly, one can predict that two thirds of patients who develop delayed primary attacks will do so nineteen to sixty-three days following the discontinuance of suppressive medication. It must be appreciated, however, that in rare cases the delayed primary attack occurs as long as one year after discontinuance of quinacrine suppression.

INITIAL PARASITEMIA

It was pointed out above that malaria smears are frequently negative at the onset of symptoms in

THE DELAYED PRIMARY ATTACK OF VIVAX MALARIA*

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DURING the war, American troops stationed in areas where malaria is endemic received quina-crine (Atabrine) or quinine for suppression of malaria, the vast majority receiving the former. A great number of these men were completely free of clinical manifestations of the disease throughout the period of suppression, but after the discontinuance of suppressive medication, the first attacks of malaria occurred. Nearly all the first, or delayed primary, attacks were vivax malaria. Falciparum malaria, with few exceptions, is definitively cured by an effective suppressive regimen of quinacrine if medication is continued for three weeks or more after the last possible infection, vivax malaria is not similarly curable.

In vivax malaria, the symptoms and signs of an acute attack can be well controlled by quinacrine or quinine, but the infection is not eradicated and recurs in a great percentage of cases. The failure of the drugs to effect a complete cure of vivax infections is reflected in the occurrence of delayed primary attacks, as well as of later relapses. The delayed primary attack itself may be regarded as the recurrence of an infection acquired earlier under conditions in which the clinical manifestations were suppressed by antimalarial agents. Despite the basically similar nature of delayed primary attacks and later relapses, the former display distinctive features, which are considered in this paper.

The problem of the occurrence of delayed primary attacks in the United States will not disappear with the end of the war. With more extensive use of suppressive medication in endemic areas and with increasingly frequent travel by American residents to and from such areas, a continued, although lower, incidence of delayed primary attacks can be expected.

MATERIAL AND METHODS

All the patients observed in this study were military personnel infected with vivax malaria of Pacific origin. Detailed observations were made in 169 cases of delayed primary attacks and in 486 cases of later relapses. The two groups were studied under the same conditions.

All patients were admitted for special treatment as soon as possible after the onset of the attack. No patient was treated unless the temperature had risen above 100°F and a smear of the peripheral blood was positive for malaria parasites. Antimalarial therapy was begun on the morning following admission. The drugs and dosage schedules were as follows: quinacrine, 2.8 gm in seven days (1.0 gm the first day and 0.1 gm three times a day

for six days), chloroquine (SN 7618)^{1, 2}, 2.0 gm. in seven days (0.8 gm the first day and 0.2 gm daily for six days), 1.0 gm in one day, 0.8 gm in seven days (0.2 gm the first day and 0.1 gm daily for six days), 1.5 gm in four days (0.6 gm the first day and 0.3 gm daily for three days) and 1.5 gm. in three days (0.9 gm the first day and 0.3 gm daily for two days), quinine sulfate, 29.0 gm in four teen days (3.0 gm the first day and 2.0 gm daily for thirteen days), and quinine-plasmochin, 29.0 gm of quinine and 0.84 gm of plasmochin naphtho-ate in fourteen days (the former according to previous schedule, and the latter, 0.02 gm every eight hours). The ratio of delayed primary attacks to later relapses was essentially similar in the various treatment groups.

Daily observations were made of the symptoms of the attack, evidences of toxicity of the drugs used and physical findings.

Counts of malaria parasites in the peripheral blood were done twice daily, in the morning and in the afternoon, until a negative smear was obtained, after which three consecutive negative daily smears were required.[†] The great majority of parasite counts were made by the Earle-Perez³ method, which utilizes a thick blood smear, the rest of the counts were determined by the leukocyte-parasite ratio, in which a white-cell count is performed and the parasite count calculated according to the ratio of parasites to white cells in a thin blood smear. The two procedures gave similar results, although the former is much simpler.

After the completion of treatment, most of these patients were transferred to the convalescent section of the hospital, where they were observed until relapse or for a period of one hundred and twenty days from the last day of treatment. No antimalarial drugs were given during this period, and smears were examined twice weekly. The occurrence of a positive smear in association with a temperature above 100°F was considered a clinical relapse, and such patients were readmitted to the treatment ward for further study and therapy. A positive smear without fever or symptoms was regarded as a parasitemic relapse and in these cases temperature observations were made three times daily and smears were examined daily until negative, if fever supervened, the patient was admitted to the ward with a diagnosis of clinical relapse.

CLINICAL CHARACTERISTICS

Most delayed primary attacks are clinically indistinguishable from later relapses of vivax malaria.

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†All counts were performed by the Imported Malaria Studies Laboratory, United States Public Health Service, under the direction of Captain Don E. Eyles.

clearance were studied. Patients with an oral temperature above 100°F were regarded as having fever. Cases in which a temperature above 100°F represented merely the defervescence from the peak of a paroxysm on the first day of treatment were not included. An analysis of the occurrence of fever on the second day of treatment in 150 cases of delayed primary attack and 465 cases of later relapse revealed a significantly higher incidence in the former (27 cases, or 18 per cent) than in the latter (29 cases, or 6 per cent). This higher incidence may have been related to the slower parasite-clearance rate in the delayed primary attacks, as suggested by the fact that of the total of 56 patients with fever on the second day only 4 per cent were found to have negative smears on that day, whereas of 559 patients who were afebrile on the second day, 25 per cent had negative smears.

As measured by the control of fever and parasitemia, the delayed primary attack responded less readily to effective antimalarial therapy than the later relapse.

RELAPSE RATE AND INTERVAL TO RELAPSE

The efficacy of antimalarial therapy is measured not only by its control of the acute attack but also by its effect on the incidence of subsequent relapse and on the length of interval to relapse.

After treatment with one of the antimalarial drug regimens, each patient was observed until the next attack or, if no attack occurred, for one hundred and twenty days after the last day of treatment. The rate and interval to relapse within one hundred and twenty days could thus be established for each group. In view of the differences noted between the response to treatment of acute attacks in delayed primary attacks and that in later relapses, it was of interest to determine whether differences also existed in the relapse rate and the interval to relapse.

The results of such an analysis in cases followed until subsequent relapse or for one hundred and twenty days are presented in Table 4, which does

within the observation period of one hundred and twenty days.

DISCUSSION

The observations presented above indicate that repeated attacks of malaria produce a somewhat altered response to treatment of an acute attack, patients with later relapses showing a diminished sensitivity to the malaria parasite as demonstrated by the higher level of parasite density required to produce symptoms. The greater effectiveness of antimalarial agents in the control of fever and in the clearance of parasites in the later relapses is a further indication that some immunity is developed during the course of recurrent attacks. Such immunity, however, is sufficient neither to diminish the likelihood of a recurrence within one hundred and twenty days after treatment of an attack nor to cause a lengthening of the interval between relapses.

The data on the interval to the delayed primary attack following the end of suppressive medication raise some interesting questions. As pointed out above, the mean interval to the first attack in 101 cases was forty-one days, with a range of three to one hundred and four days. This wide range obtained in patients who received large doses of suppressive quinacrine as well as in those treated with the usual dosage of quinacrine. An adequate concentration of quinacrine in the plasma is necessary to maintain effective suppression of the symptoms of malaria. There is a considerable range in the plasma concentrations of quinacrine achieved on suppressive regimens, and there are corresponding variations in the time required for the concentration to drop to its minimal effective level after the cessation of medication. Such factors probably account for some of the variation in length of intervals to primary attacks, but not for the wide range of intervals observed. Symptoms do not necessarily develop as soon as the quinacrine concentration in the plasma has fallen below the minimal effective level. One of the other factors that possibly determine the interval may be the natural periodicity of recurrent vivax infections.

Many patients who had had several attacks of malaria stated that the attacks recurred at regular intervals, usually every six to eight weeks, and many followed through the course of several recurrences did show such periodicity. If one assumes a normal variation among patients in the length of the periods between attacks and differences in the periodicity of various strains of vivax parasites, the wide range in the intervals to delayed primary attacks becomes understandable.

During the course of suppression there may be recurrent episodes of malarial activity in which the clinical manifestations are not evident so long as the plasma concentration of quinacrine remains at an effective level. When suppression is discontinued

TABLE 4. Relapse Rate and Mean Interval to Relapse Following Treatment of Delayed Primary Attacks and Relapses

TYPE OF ATTACK	NO OF CASES	CLINICAL RELAPSE WITHIN 120 DAYS		MEAN INTERVAL TO RELAPSE <i>days</i>
		NO OF CASES	PER- CENTAGE	
Delayed primary attack	109	76	69.7	54.4
Later relapse	259	193	74.6	53.2

not include patients treated with combined quinine and plasmochin, in whom the incidence of relapse within one hundred and twenty days is less than 10 per cent.⁵ The rates of relapse and the mean intervals to relapse were nearly identical in both groups, as was the distribution of intervals to relapse.

delayed primary attacks This observation indicated that some patients in the primary attack are unduly sensitive to the malaria parasite and have a marked clinical reaction to low parasitemic levels This occurrence is more frequent in the delayed primary attack than in relapses An analysis was made of the parasite counts taken in the morning of the first day of treatment prior to the administration of the

reported counts of less than 1000 per cubic millimeter at the onset in 47 of 50 patients in whom Pacific vivax malaria was induced by means of infected mosquitoes A large proportion of patients with a parasite density of less than 1000 per cubic millimeter have thin smears that are completely negative or show extremely rare parasites These findings indicate the importance of thick smears for the detection of malaria, particularly in the primary attack

TABLE 2 Interval Between End of Suppression and Onset of Delayed Primary Attack

NO OF PATIENTS	SUPPRESSIVE QUINACRINE DOSAGE	RANGE OF INTERVAL	MEAN INTERVAL
	gm. per week	days	days
19	Less than 0.7	3 to 87	41.5
55	0.7	8 to 104	42.2
21	More than 0.7	10 to 83	39.9

first dose of drug The frequency distribution of initial parasite densities in delayed primary attacks and relapses is presented in Figure 1

It is evident that the level of parasitemia at the onset of an attack is significantly lower in the delayed primary attack than that in the later relapses Fifty-four per cent of the delayed primary cases

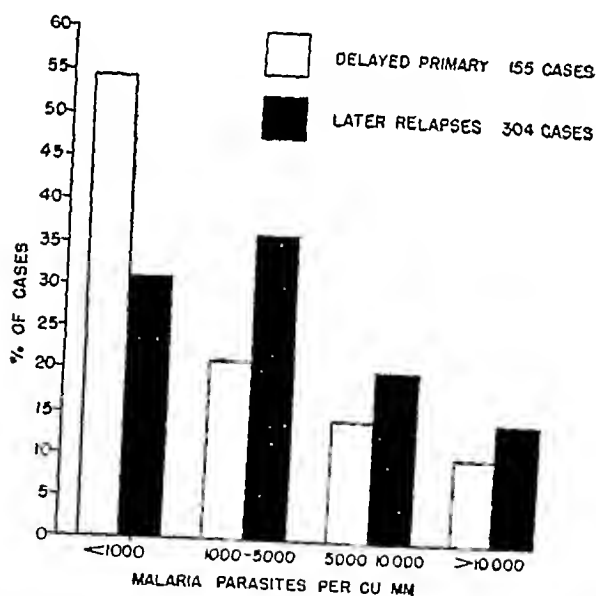


FIGURE 1 Initial Parasite Densities in Delayed Primary Attacks and Relapses of Pacific Vivax Malaria

had counts less than 1000 per cubic millimeter, whereas this was true in only 31 per cent of later relapses These findings are in agreement with the clinical impression that the majority of patients in the former group show a greater symptomatic reaction to low parasite concentrations than those in the latter Low parasite concentrations in primary attacks were observed by Eyles and Young,⁴ who

PARASITE CLEARANCE RATE

It has been our experience in the treatment of large numbers of cases of vivax malaria that, on the whole, patients with low parasite counts at the beginning of treatment are more rapidly cleared of parasitemia than those with high initial parasite counts Inasmuch as the initial parasitemia is significantly lower in the delayed primary attacks than in the later relapses, one might expect that cases in the former group would be more rapidly cleared of parasites than those in the latter, the opposite, however, was observed

Table 3 presents a comparison of the rate of parasite clearance in delayed primary attacks and in later relapses The ratio of delayed primary attacks to later relapses was essentially similar in all treatment groups and offset known variations in the rates of parasite clearance by quinine, quinacrine, chloroquine or plasmochin Twenty-four hours after the beginning of treatment, only 17 per cent

TABLE 3 Parasite Clearance in Treatment of Delayed Primary Attacks and Relapses

CLEARANCE AFTER FIRST DOSE OF DRUG	DELAYED PRIMARY ATTACK (152 CASES)	LATER RELAPSES (186 CASES)
Ar	%	%
24	17	25
48	67	73
72	91	94
96	99	100
132	100	

of delayed primary cases had negative smears, whereas 25 per cent of later relapses were negative This difference is statistically significant (probability 0.029) On subsequent smears the rates of clearance were gradually equalized

CONTROL OF FEVER

The temperature course is a valuable index of the response of a malaria patient to therapy The presence or absence of fever on the second day of treatment was found to be a useful measure of this response

This measure was applied to the cases of delayed primary attack and to those of later relapse in the same treatment groups in which the rates of parasite

QUARTAN MALARIA OCCURRING SUBSEQUENT TO A BLOOD TRANSFUSION*

Report of a Case

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CASE REPORT

WITH the return of military personnel from areas where malaria is endemic, the problem of post-transfusion malaria is bound to assume greater importance than it has in the past. The following case deserves mention because of several unusual features.

E M., a 40-year-old married woman, was admitted to the Rhode Island Hospital on February 25, 1946, complaining of chills and fever every 3rd day for the last several weeks she had previously been seen at the hospital on September 19, 1945, when she was admitted in shock. At that time she gave a history of vaginal bleeding for 1 week and profuse bleeding for 3 days following self-attempted uterine instrumentation. While in the hospital she received three 500-cc transfusions of stored blood and 1 unit of plasma. With penicillin and supportive treatment she made an uneventful recovery and was discharged on the 10th hospital day. Following her return home she had considerable irregular vaginal bleeding, but she gained weight and strength and was able to do her housework adequately. At about 7:00 p.m. on November 23, after a short period of malaise, she suddenly experienced a severe shaking chill, which lasted about 2 hours. This was followed by severe drenching sweat, backache and headache, which had entirely disappeared by the following morning. On November 26 malaise and a chill, followed by sweating, backache and headache, returned. She was seen by a physician, who was aware of the cause of her recent hospitalization and who gave her one of the sulfonamides—it was estimated that she took about 7 gm daily for 4 days. During the month of December, there was only 1 episode of chill and fever, which occurred about the middle of the month. The febrile episodes began again on January 12 and occurred at irregular intervals throughout the month. The patient had no symptoms during the first week in February but on February 8 there was a recurrence of chills and fever. From that time until 2 days before admission to the hospital, the chills and fever occurred regularly every third day at a time that the patient was able to predict.

There was no family or past history of malaria, tuberculosis, diabetes or cancer. The patient was born in Vermont, where she had lived for about 37 years before moving to Providence, and had never been outside the New England states. Her health had always been good, except for scarlet fever in childhood and an appendectomy and right salpingo-oophorectomy at the age of 14. She had had twelve pregnancies, 8 babies having been delivered at term, with four pregnancies terminated by induced abortion.

Physical examination revealed a rather thin but well developed woman who appeared well. The temperature, pulse and respirations were normal. The blood pressure was 110/70 in each arm. The examination was entirely negative, except that the oral mucous membrane appeared slightly pale. The liver was not palpable and was percussed at the costal margin on deep inspiration. The spleen was not felt.

On the day of admission, x-ray examination of the chest was reported as negative, and the urine was said to contain a trace of albumin and a trace of sugar.

At about 1:00 p.m. on the 2nd hospital day, just as the patient had predicted, she began to have malaise, backache and headache. These symptoms progressed, and the temperature rose, about 2 hours later she was at the height of a moderately severe paroxysm, with an oral temperature of

105°F. A thick blood film, which was taken during the paroxysm and reported as negative for malarial parasites, was later reviewed and showed quartan parasites, *Plasmodium malariae*. Examination of the blood showed a red-cell count of 3,700,000, with a hemoglobin of 12.6 gm, and a white-cell count of 5950, with 74 per cent neutrophils, 20 per cent lymphocytes and 6 per cent monocytes. The parasite density during the paroxysm, as determined from the original blood film by the method of Watson,¹ was 60 organisms per cubic millimeter. The blood urea nitrogen was 7 mg and the blood sugar 77 mg per 100 cc. The blood Hinton reaction and agglutinin tests for typhoid, undulant and typhus fever were negative. A blood culture was sterile. An electrocardiogram was within normal limits. By 7:00 p.m. the patient was much improved, and by the next morning, except for slight weakness, she was entirely free of symptoms.

At 8:30 p.m. on the 4th hospital day blood films revealed a parasite density of 1566 organisms per cubic millimeter. The white-cell count was 4450. Earlier in the day, an intravenous pyelogram had been reported as normal. At 9:30 a.m. on the 5th hospital day the parasite density was 576 organisms per cubic millimeter, and examination of the blood showed a red-cell count of 4,270,000, with a hemoglobin of 11.3 gm, and a white-cell count of 5450 with 48 per cent neutrophils, 49 per cent lymphocytes and 3 per cent monocytes. The urine showed a trace of albumin but no bile and a urobilinogen concentration of 0.65 mg per 100 cc. The blood urea nitrogen was 8 mg, the blood sugar 77 mg, and the blood cholesterol 118 mg per 100 cc, and the icteric index was 4.2.

As expected, in the afternoon, the patient experienced a malarial paroxysm almost identical to the previous one. At what was judged to be the height of this episode the parasite count was 410 organisms per cubic millimeter. Examination of the blood showed a red-cell count of 4,260,000 and a white-cell count of 4500 with 53 per cent neutrophils, 46 per cent lymphocytes and 1 per cent monocytes. At that time a blood volume determination was done with the dye T-1824,² the 10-minute sample method of Gregersen,³ as modified to the use of the Cencophotometer, being used. The dye was injected by means of a calibrated syringe. Hematocrit determinations on venous blood were done in Wintrobe tubes, and plasma protein determinations by the method of Bowman⁴ were performed on the control and dye samples. These determinations were repeated on the 11th hospital day, after 6 days with no fever or symptoms (Table 1). Quinacrine, 0.2 gm by mouth, was begun at 4:00 p.m. It was planned to continue this dosage every 6 hours for five doses for a total of 1 gm. The patient received 1.4 gm in 0.2-gm doses in the succeeding 48 hours. The dosage then was changed to 0.1 gm three times daily for five more days. The total dosage was 2.9 gm.

At 9:00 a.m. on the sixth hospital day, the parasite density was 432 organisms per cubic millimeter, and examination of the blood showed a red-cell count of 3,950,000, with a hemoglobin of 11.5 gm, and a white-cell count of 3600, with 57 per cent neutrophils, 29 per cent lymphocytes, 13 per cent monocytes and 1 per cent eosinophils. The urine contained no bile, and the urobilinogen concentration was 0.4 mg per 100 cc.

At 10:00 a.m. on the 7th hospital day the parasite density was 450 organisms per cubic millimeter, and the white-cell count was 4500.

On the 8th hospital day—the 4th day of quinacrine treatment—no parasites were seen in the thick blood film. Examination of the blood showed a red-cell count of 3,910,000 with a hemoglobin of 11.5 gm, and a white-cell count of 5500, no differential count was done. On the 10th hospital day examination of the blood showed a red-cell count of 4,150,000, with a hemoglobin of 11.5 gm, and a white-cell count of 4200, with 63 per cent neutrophils, 32 per cent lymphocytes, 4 per cent monocytes, and 1 per cent eosino-

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and the plasma concentration declines below the effective level, a clinical attack becomes possible. But the time of occurrence may depend on the periodicity of the infection in individual cases and the relation of the last preceding episode of suppressed malarial activity to the date of the last effective quinacrine concentration in the plasma. Thus, if a period of suppressed activity occurs immediately before the end of suppression, the delayed primary attack usually does not follow for another six to eight weeks. If the periodicity is longer, the attack may not occur until as long as one hundred days later. In cases in which the interval to the first attack is even longer, it is possible that one or more periods of subclinical malarial activity occur before a full-blown clinical attack develops. If a period of activity is due immediately after the discontinuance of suppressive medication in a patient who is highly sensitive to the malaria parasite, the delayed primary attack may readily occur within the first week after the end of suppression.

These considerations, although speculative, seem best to explain the wide range of intervals to the first attack observed following cessation of suppression.

SUMMARY

In this study, based on 169 cases of delayed primary attacks and 486 later relapses occurring in military personnel with vivax malaria of Pacific origin, most of the delayed primary attacks were clinically indistinguishable from later relapses. Occasionally, however, such attacks posed problems in diagnosis. Treatment with sulfonamides, penicillin or antimalarial drugs should be withheld until a diagnosis is established. The existence of malaria should be proved by positive blood smears, so that rational treatment can be instituted and subsequent malaria attacks can be promptly recognized and properly treated.

The mean interval between the cessation of suppression and the onset of the delayed primary attack in 101 cases was forty-one days. One can predict that two thirds of delayed primary attacks will occur between approximately the third and the ninth week after the end of suppression.

The parasite concentrations in the peripheral blood were significantly lower at the onset of delayed primary cases than those in later relapses. Accordingly, thick-smear examinations should be made at least twice daily until parasites are found.

The rate of parasite clearance under treatment was somewhat slower in the delayed primary attack than in the later relapse, despite the lower initial parasite counts.

Fever was less readily controlled in the delayed primary attack than in later recurrences.

The incidence of clinical recurrence within one hundred and twenty days after treatment of the acute attack was essentially the same for delayed primary cases and later relapses. The mean interval to relapse was also nearly identical in both groups, as was the distribution of intervals to relapse within the observation period of one hundred and twenty days.

The higher initial parasitemia in later relapses suggests a diminished sensitivity to the malaria parasite. This finding, in addition to the more rapid parasite clearance and control of fever that occur in the treatment of later relapses, indicates the development of some immunity in the course of recurrent vivax malaria infection.

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ved in the United States for thirty-two years. The other, who gave a history of malaria in childhood, had lived in Michigan for thirty-six years. Blood smears were examined for malaria on one occasion in both donors, but no parasites were seen.

Sharnoff, Geiger and Seltzer⁶ reported 2 cases of malaria following the transfusion of stored blood. One of them was the quartan type. The 3 donors involved in this case were natives of New Jersey, the British West Indies and Puerto Rico, respectively. Blood samples from these donors were stored eight, two and eight days, respectively. The other case was tertian (vivax) malaria. The donor involved was a Puerto Rican, and the blood had been stored for two days.

With the exception of the case presented above, no cases of malaria subsequent to blood transfusion have been reported from the blood bank of the Rhode Island Hospital, which from May, 1942, to January 1, 1946, supplied blood for about forty-five hundred transfusions.⁷

Of the 3 donors involved in this case, 2 were Italian born. One was a fifty-six-year-old native of Naples, who gave a history of malaria that had been treated with quinine forty years previously. He had subsequently been free of the symptoms of malaria and had lived in New England ever since his immigration thirty years previously. The second donor, a fifty-seven-year-old native of Brindisi, gave a history of malaria treated successfully with quinine forty-six years previously and stated that he had been free of the symptoms of malaria ever since that time and had lived in New England since his immigration ten years later. The third donor, a fifty-five-year-old native of Providence, stated that between the ages of six and thirteen years she had had malaria every summer. These attacks had all been treated with quinine and had not recurred in the last forty-two years.

Thick blood films were examined once in all 3 donors, and twice in 1, but no malarial parasites were seen. The blood used for the transfusions had been stored at a temperature of 6°C for five days in the first donor, seven in the second, and twelve in the third. In this reported case the length of time between the transfusions of blood and the appearance of the clinical symptoms of malaria was sixty-six days.

In the clinical study of this case, two features were of especial interest. The first was that low parasite densities were maintained during the period of study (Fig 1). Kitchen⁸ states that *P. malariae* appears to be more toxic, in relation to parasite density attained, than either *P. vivax* or *P. falciparum*. The second feature was that blood-volume determinations, one made during a paroxysm and another in convalescence six days later, showed no significant alterations in the plasma, blood or circulating erythrocyte volumes (Table 1). Feldman and Murphy⁹ described blood plasma and erythrocyte changes occurring in infections with *P. vivax* and *P. falciparum* that reflect the response of the body to erythrocyte destruction. The absence of significant erythrocyte destruction, owing to the low parasite densities attained, may explain the absence of significant blood-volume changes in the case reported.

SUMMARY

A case of quartan malaria, caused by *Plasmodium malariae*, in a native of New England subsequent to the transfusion of stored blood is reported. The three donors involved gave past histories of malaria forty, thirty-six and forty-two years previously, but blood films failed to reveal malarial parasites.

The course of the illness, the parasite densities attained, the white-cell counts and the response to quinacrine therapy are discussed.

Plasma, total blood and erythrocyte volumes, determined with the dye T-1824, were essentially the same during a paroxysm as during convalescence.

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phils. On the 11th hospital day no parasites were seen in the thick blood film. The blood cholesterol was 140 mg per 100 cc, and the icteric index was 3.3. The urine showed a concentration of urobilinogen of 0.1 mg per 100 cc.

At no time during the hospital stay was the spleen palpable, and only once was the liver edge felt at the costal margin on deep inspiration. The patient was discharged on the 14th hospital day, and when seen in follow-up on April 6, she stated that she had had no further symptoms of malaria.

Figure 1 shows the relations of the fever and pulse rate to the parasite densities and the white-cell count and the response to quinacrine treatment.

Rubenstein, Shulman and Merrill⁴ reported 12 cases of malaria occurring subsequent to blood trans-

fusion where insect transmission does not exist or is extremely rare as the known period of latency of the malarial infection, whether or not the donor presents a history of malaria. In the 5 donors in whom the duration of latency of the malarial infection was established, it varied from twelve to twenty-seven years. Not one of these donors had a history of manifest malaria. The duration of latency of infection in 3 donors with a history of malaria could not be stated. One of the 3 had a positive blood film for malaria. The other positive blood film was found in a patient with no history of malaria. In 8 of the

TABLE 1 Blood-Volume Determinations with T-1824

HOSPITAL DAY	TEMPERATURE	HEMATOCRIT		PLASMA PROTEIN		BLOOD VOLUME		PLASMA VOLUME		ERYTHROCYTE MASS	
		MEASURE	CHANGE	MEASURE	CHANGE	MEASURE	CHANGE	MEASURE	CHANGE	MEASURE	CHANGE
	°F	%	%	gm per 100 cc	%	cc	%	cc	%	cc	%
Fifth	105	37.4		6.4		4630		2900		1730	
Eleventh	98.6	38.6	+3	6.7	+5	4500	-3	2754	-5	1746	+1

fusion in Massachusetts since 1929. Six cases were reported during the years 1939 to 1944, and at least 9—possibly 10—of the cases were quartan in type. Ten of the 12 donors involved in the study had lived for a period of years in a country where malaria is known to be endemic. In the other 2

cases of quartan malaria reported by these authors, the incubation period varied from twenty-one to one hundred and eleven days, with an average of fifty-two days.

McClure and Lam⁵ reported 2 cases of quartan malaria subsequent to the transfusion of blood that

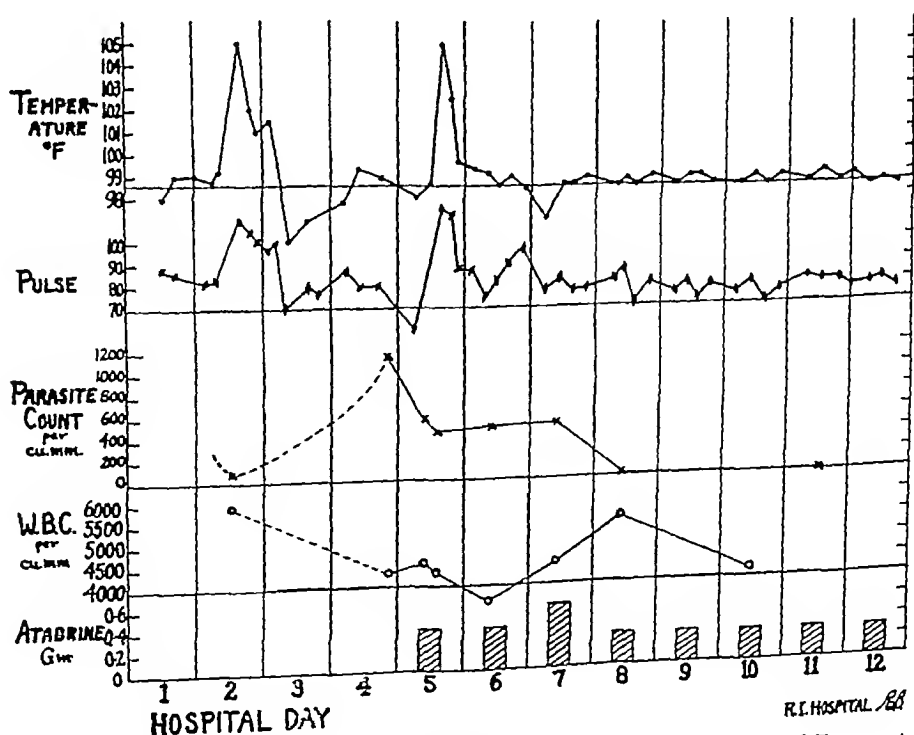


FIGURE 1 Relation of Clinical Course to Parasite Densities, White-Cell Count and Treatment with Quinacrine

cases information concerning the donor's country of residence was not available. The authors regarded the length of time of residence in a new country

had been stored, in each case, for five days. Both donors had been born and had spent their childhood in Sicily. One, who gave no history of malaria, had

As might be expected previous gravidity was more frequent in the older than in the younger patients. Of those over thirty-five years of age 84 per cent had been gravid, and of those between twenty-five and thirty-five 78 per cent had been gravid, whereas of those under twenty-five only 54 per cent had been gravid. This is one of the

or both. Operative cases in which any portion of the adnexa remained after conservative surgery were regarded as improved rather than cured, owing to the potentiality of involvement of the remaining adnexa, cure in such cases implied complete removal of adnexa, including all the diseased tissue, and complete relief of symptomatology.

TABLE 1 *Results of Treatment*

TREATMENT	AGE GROUP	NO OF CASES	HOSPITAL STAY days	NO IM- PROVEMENT	IMPROVEMENT	CURE	DEATH
Bed rest alone	yr						
	Under 25	66	13 3	1	65	0	0
	25-35	34	13 4	2	27	5	0
	Over 35	8	21 0	0	6	2	0
Totals	-	108		3 (3%)	98 (91%)	7 (6%)	0
Average	-		15 9				
Bed rest and sulfonamides	Under 25	93	13 8	3	86	4	0
	25-35	36	15 8	1	29	4	2
	Over 35	19	16 1	1	17	1	0
Totals	-	148		5 (3%)	132 (89%)	9 (6%)	2 (1%)
Average	-		15 2				
Bed rest and surgery	Under 25	7	19 4	0	5	2	0
	25-35	19	24 5	0	13	6	0
	Over 35	15	21 9	0	8	7	0
Totals	-	41		0	26 (63%)	15 (37%)	0
Average	-		21 9				

reasons for the policy of conservatism in the younger group whenever possible.

All patients were kept in bed and received routine nursing care, with the occasional use of codeine and aspirin for relief of pain. Patients who received sulfonamide therapy were given sulfanilamide or sulfadiazine, or both. The daily dosage varied from 3 to 4 gm, along with an alkali—usually sodium bicarbonate—in suitable dosage.

If one assumes that 25 mm in one hour by the Westergren technic is the normal upper limit of the blood sedimentation rate, 131 cases (44 per cent) were above and 166 cases (56 per cent) were below this level on admission to the hospital.

The chief complaints in the entire series were as follows: pelvic pain, 95 per cent, vaginal discharge, 33 per cent, bleeding, 10 per cent, urinary frequency, 10 per cent, and backache, 10 per cent.

To our knowledge, three errors in diagnosis were made, all in cases diagnosed as acute appendicitis that were in fact pelvic inflammatory disease.

The indications for operation in these cases were persistence of masses or of subjective symptoms or both. A prerequisite for operative interference in most cases was a sedimentation rate of 25 mm or less, to give assurance that active infection was not present.

RESULTS OF TREATMENT

The results of the various forms of treatment are presented in Table 1.

In classifying the cases, improvement consisted in relief of symptoms or subsidence of the disease,

In unoperated cases, cure consisted in complete resolution of all obvious disease and disappearance of all symptoms.

Experience indicated that many patients regarded as improved later had recurrences of the disease.

The following are brief summaries of the 2 fatal cases.

CASE 1 A 26-year-old Negress who had had four pregnancies and given birth to 2 children was admitted to the hospital with acute pelvic inflammatory disease and peritonitis. The sedimentation rate varied from 25 to 100 mm. The patient was given transfusions, infusions, sulfathiazole and sulfadiazine. There was an elevation in temperature daily up to 103°F. The patient progressively failed, dying on the 22nd hospital day of peritonitis.

CASE 2 A 26-year-old Negro primipara was admitted to the hospital with septic, incomplete abortion, parametritis and thrombophlebitis of the pelvic veins. The uterus was evacuated with sponge forceps. Seven small blood transfusions, as well as sulfathiazole and sulfanilamide were given. The patient died on the 73rd hospital day of septic pulmonary emboli and abscess formation.

An interesting observation is that over four fifths of the cases in this series of pelvic inflammatory disease occurred in women under thirty-five and more than half in women under twenty-five years of age. This fact suggests that such disease is characteristic of the early part of sexual life.

The use of sulfonamides appeared to have no influence on the average period of hospital stay, which in patients treated with bed rest alone was almost identical with that in patients treated with

PELVIC INFLAMMATORY DISEASE*

A Survey of 300 Consecutive Cases, with Special Reference to Treatment

JOHN E. TRITSCH, M.D.,† IRVING H. SAXE, M.D.,‡ AND EDWARD SCHNEIDER, M.D.§

NEW YORK CITY

THE sulfonamides have become well established as invaluable agents in the treatment of many infective conditions. As a result, the tendency has been to regard the drugs equally effective in any infective state, and they are given routinely by many physicians whenever a febrile inflammatory condition develops.

For some time, we had doubted the value of the sulfonamides in many of the cases of pelvic inflammatory disease under our care at the Metropolitan Hospital. We therefore examined the literature to determine the experience of others in the use of the drugs in such diseases.

As early as 1938, Gillett¹ believed that sulfanilamide was 100 per cent effective in the treatment of acute salpingo-oophoritis without demonstrable inflammatory masses and in recurrent acute salpingo-oophoritis. He conceded, however, that there was little, if any, improvement if adnexal masses were present.

In 1938, Goff² stated that vigorous sulfanilamide therapy within the first two or three days of an acute gonorrheal infection completely aborted the process in most cases, but that a permanent cure did not necessarily follow. He reported that in patients seen late in the course of infection an occasional pelvis cleared up but that in most cases some residual infection remained. He believed that probably 50 per cent of cases eventually required operation—an operative incidence much higher than that in the cases in this study.

In 1941 Williams³ compared the effect of sulfanilamide therapy on 72 patients with acute pelvic inflammatory disease with that obtained in 100 patients treated similarly except that the drug was not given. He concluded that the dramatic results often obtained with sulfanilamide in streptococcal infections and in pneumonia were disappointingly absent. He stated that, if given early, the drug prevented the development of tubal involvement in gonorrheal infection but was of little value once the inflammatory process in the adnexa had become well established.

Barrows and Labate,⁴ in 1943, studied 204 cases of acute salpingitis treated with sulfanilamide and sulfathiazole, of which 71 were primary and

133 acute exacerbations. They found that primary attacks of less than five days' duration were apparently cured after a week of chemotherapy in 70 per cent of the mild and 66 per cent of the moderate cases, with resolution of adnexal masses. Mild and severe cases of longer duration and recurrent cases showed no adequate response.

In a study of pelvic inflammatory disease of specific origin, Miller⁵ asserted that, except for general measures, no treatment of pelvic inflammatory disease gives satisfactory results, chemotherapy being disappointing in infections above the internal cervical os. He also stated that surgery is ultimately necessary in a large proportion of cases of recurrent salpingitis, particularly in public institutions with a large number of Negro patients, and that conservative surgery must frequently be followed by secondary surgery. Acute appendicitis furnished the chief difficulty in differential diagnosis. He concluded that bacteriologic diagnosis, whether by smear or culture, is highly unsatisfactory.

It was thus evident that our opinion was—at least in part—shared by others, and a survey of our own cases at the Metropolitan Hospital was undertaken. It was decided to analyze a large number of consecutive cases of pelvic inflammatory disease without attempting to classify the type of disease or the cause. The patients had two things in common: all had inflammatory disease of the pelvis and all were ill enough to be hospitalized. Some were desperately ill, and 2 died. Some of these patients were treated by bed rest alone, others by bed rest and sulfonamides and still others by bed rest and surgery.

GENERAL CONSIDERATIONS

The youngest patient in the series was thirteen and the oldest fifty-two years of age. One hundred and sixty-seven patients (56 per cent) were under twenty-five, 90 (30 per cent) were between twenty-five and thirty-five, and only 43 (14 per cent) were over thirty-five.

Two hundred and sixteen patients (72 per cent) were Negroes. This was chiefly due to the fact that the district served by the hospital is largely populated by Negroes, but other factors, such as social and economic status, played a definite role. Because of this racial distribution, most of the patients in this series were probably more neglected than the average patient, with a higher morbidity, mortality and need for operation.

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Dermatitis in the form known as eczema is by far the most frequent of the occupational dermatoses. Dermatitis is an inflammation of the skin due to internal or external factors, the result of contact, ingestion, inhalation, injection, instillation or some other method of absorption.⁴ The lesions, which are characterized by erythema, edema, papules and vesicles, may progress to simple scaling and desquamation or may become oozing and crusted and then desquamate, they may become secondarily infected with pustules or persist as infiltrated, excoriated, lichenified eruptions that prove resistant to treatment. Any one of the lesions, or any combination, may be present.

Occupational dermatoses are with few exceptions due to external agents. Dermatitis from such causes (dermatitis venenata) is so frequent that it requires classification. This classification considers first the type of agent, second the use of this agent and third the nature of the lesions produced. The second division is of little value because the agent may be employed under continually changing conditions, for example, paraphenylenediamine is extensively used in the manufacture of cosmetics, textiles and garments and in other branches of industry. The third division is also open to criticism because the same agent may produce varying degrees of disease depending on its strength as applied, the area to which it is applied and the method of application — that is, the degree of friction involved and the length of the period of exposure. An example is that of oils that cause folliculitis of the arms or cancer of the scrotum.

In general, the concentration of the irritant, the length of time it is applied and the condition under which exposure occurs serve to differentiate two types of dermatitis venenata — nonsensitization and sensitization. Just where the former ends and the latter begins is often impossible to determine. Nonsensitization dermatitis is caused by an irritant that affects practically all human skins. The irritant may be a mechanical or physical agent or a powerful chemical applied, either deliberately or accidentally, to the skin. The reaction is sudden and explosive. It is characterized by all degrees of inflammation and at times by the destruction of the cutaneous layers and even the subjacent tissues. The causative factor is almost always recognized and known to the patient, hence, recovery is fairly

prompt, for with removal of the cause the eruption heals rapidly with little or no treatment. Eczema, variously known as sensitization dermatitis, contact dermatitis or contact eczema and allergic dermatitis or allergic eczema is an inflammation of the skin due to repeated exposures to substances that are normally innocuous. In this type of disease there is an initial exposure without resulting lesions, but subsequent exposures to even minimal quantities of the substance involved may result in reactions, manifested either at the local site of contact or as a generalized process. Every eczema is a dermatitis, but the converse is not true.

The actual causes of occupational dermatoses include mechanical, physical and chemical agents, flowering plants and their products and biologic agents. The chemical causes are divided into primary irritants and sensitizers.

A primary irritant is defined by the Council on Industrial Health¹ as follows: "When a substance in a given concentration, in a given vehicle and after a given manner and length of exposure produces clinically manifested irritation on the skin of the majority of persons not previously sensitized to that substance, then that substance is a primary irritant under the specified conditions." Primary irritants usually cause dermatitis after the first contact. They are the strong acids, alkalis, certain salts of heavy metals, solvents, essential oils, dye intermediates and some oils and greases.

A sensitizer is a substance that does not necessarily cause demonstrable cutaneous changes on the first contact but may effect such specific changes in the skin that, after five to seven days or more, further contact on the same or other parts of the body causes dermatitis. Sensitizers are chemicals that are innocuous to most skins. Sensitization may occur after a latent period of varying length — from days or weeks to months or even years.⁵ The important sensitizers are resins, plastics, dyes, oils, soaps, accelerators, explosives, insecticides, plants, drugs and cosmetics. Experimentally no agent has been proved to be of value in desensitizing susceptible persons. It has, however, been the experience of one of us (J. G. D.) that in some industries the worker may become more or less resistant to outbreaks from contact with these substances and be able to continue his work, but that if he stops work and then returns to the same exposure, he may have an explosive recurrence of his eruption. Regarding this resistance there is apparent disagreement. Schwartz⁶ has labeled this phenomenon "hardening," which he describes as the disappearance or the failure of reappearance of an allergic contact type of dermatitis in sensitized persons on repeated exposure in industry to the sensitizing chemical.

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Improvement obtained with bed rest alone when compared with that afforded by bed rest and sulfonamides showed little difference—91 per cent in the former and 89 per cent in the latter. The small number of patients regarded as cured is outstanding evidence of the inadequacy of these methods of treatment. Cure was obtained in 6 per cent of cases both with bed rest alone and with bed rest and sulfonamides. The percentage of cures in the operative cases was higher, sixty-three per cent of patients being improved and 37 per cent cured. There were no deaths in the operative series.

SUMMARY

A group of 297 patients with pelvic inflammatory disease was studied. The incidence of disease

was much greater in the younger than in the older age group, decreasing progressively with age. Pelvic pain and discharge constituted the most frequent chief complaints.

The therapeutic results obtained with bed rest alone and with bed rest with the administration of sulfonamides were practically the same, as determined by the period of hospital stay and the condition of the patient on discharge.

The incidence of surgical interference in the entire series was low (14 per cent) and was progressively lower in the younger age groups.

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MEDICAL PROGRESS

OCCUPATIONAL DERMATOSES

J. G. DOWNING, M.D.,* AND S. J. MESSINA, M.D.†

BOSTON

INDUSTRIAL medicine made remarkable progress as a result of World War I and World War II. Unprepared in 1917, it rapidly learned by trial and error, so that during the last few years of the later conflict, through preparation and research, it was able to maintain pace with the tremendous production of industry in wartime. Early recognition of the problems of health and hygiene contributed in no small part to the splendid industrial achievement in the United States. Prevention of industrial affections, by the control and elimination of hazards, enabled industry to perform almost a miracle, not only with less manpower but also with personnel less physically fit.

The skin received the first onslaught of industrial exposures. Dermatologists, especially those previously trained in industrial dermatology, were overwhelmed with work involving care of workers, inspection of plants and consultations with sanitary

engineers and insurers. The results of their efforts at control and prevention, especially in cutting oil hazards, rapidly became evident. The groundwork and teachings of the various committees for investigation of occupational dermatoses of the Council of Industrial Health of the American Medical Association early produced excellent results. The field work and publications of the Section of Dermatoses Investigation of the United States Public Health Service merit great commendation for its achievement. It is hoped that a vast amount of knowledge and statistics have naturally resulted from these efforts, and that the chemicals designed for human destruction may now be put to the advantage of the human race. Already, lethal gases and radioactive substances have been tried experimentally in the cure of fatal diseases such as leukemia and Hodgkin's disease.

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A primary irritant is defined by the Council on Industrial Health¹ as follows "When a substance in a given concentration, in a given vehicle and after a given manner and length of exposure produces clinically manifested irritation on the skin of the majority of persons not previously sensitized to that substance, then that substance is a primary irritant under the specified conditions" Primary irritants usually cause dermatitis after the first contact They are the strong acids, alkalis, certain salts of heavy metals, solvents, essential oils, dye intermediates and some oils and greases

A sensitizer is a substance that does not necessarily cause demonstrable cutaneous changes on the first contact but may effect such specific changes in the skin that, after five to seven days or more, further contact on the same or other parts of the body causes dermatitis Sensitizers are chemicals that are innocuous to most skins Sensitization may occur after a latent period of varying length — from days or weeks to months or even years⁵ The important sensitizers are resins, plastics, dyes, oils, soaps, accelerators, explosives, insecticides, plants, drugs and cosmetics Experimentally no agent has been proved to be of value in desensitizing susceptible persons It has, however, been the experience of one of us (J G D) that in some industries the worker may become more or less resistant to outbreaks from contact with these substances and be able to continue his work, but that if he stops work and then returns to the same exposure, he may have an explosive recurrence of his eruption Regarding this resistance there is apparent disagreement Schwartz⁶ has labeled this phenomenon "hardening," which he describes as the disappearance or the failure of reappearance of an allergic contact type of dermatitis in sensitized persons on repeated exposure in industry to the sensitizing chemical

In plants manufacturing or using synthetic resin varnishes, there is a high incidence of sensitization dermatitis Incompletely cured or incompletely polymerized resins and byproducts are responsible

for the eruption. Patch tests made with this material on workers suffering from dermatitis or who had an eruption due to contact with the synthetic resins elicited positive reactions. Other workers who were free from any skin eruption but who had previously had a sensitization dermatitis gave negative reactions.

Among workers with tetryl, 56 (11 per cent) of 500 employes in one plant developed dermatitis. In another 1905 (30 per cent) of 6364 workers developed dermatitis, and 1618 (85 per cent) of them returned to work with no further trouble. In a plant manufacturing TNT (trinitrotoluol), 10 per cent of the workers developed dermatitis, and all were able to return to work.⁴ Probst and his associates,⁵ on the other hand, found that tetryl workers did not develop tolerance. In aircraft workers suffering eruptions from dural, aluminum or zinc chromate primer, Hall⁷ encountered no tolerance.

Hardening may be permanent but usually disappears if exposure is discontinued for any length of time. The degree of hardening varies. Exposures to higher concentrations of the sensitizing agent than that to which tolerance has been established may cause a recurrence of the dermatitis.

No attempt is made to present a complete review of all the causes of occupational dermatoses, since only the literature of the last few years is covered. Many causes are so well known and have been so completely eliminated from industry — for example, arsenic in the wallpaper industry — that the subject matter has been divided not according to occupation but according to the offending agent. A brief description of the occupations employing the particular irritant and of the cutaneous reactions to it follows.

MECHANICAL AND PHYSICAL AGENTS

Vibrating Tools

Gurdjian and Walker⁸ reported the occurrence of a circulatory disturbance of the hands of 6 women who used pneumatic hammers. After a few months to several years of exposure to the vibrations, the patients noted attacks of blanching and numbness of the fingers. In right-handed persons, the little, ring, middle and, sometimes, the index finger of the left hand and the tips of the fingers of the right hand were involved. The vibrating tool was held in the left hand, so that in left-handed persons the condition of the hands was reversed. The attacks of blanching often occurred during work, but usually came early in the morning or during washing, especially in cold weather. The condition is known by various names — dead fingers, white fingers, Raynaud's disease and traumatic vasospastic syndrome.

Hunter and Perry⁹ observed white fingers in riveters, caulkers and fettlers using vibrating tools. Telford, McCann and MacCormack¹⁰ reported "dead hands" in users of vibrating tools. Thirty-four cases

developed after six to forty months' use of high speed vibrating tools. These authors recommend that workers who have handled such tools for nine months stop this type of work.

The industries employing pneumatic hammers, high-speed vibrating tools (those operating at 2000 to 3000 r.p.m.), chisels, riveters, road drills and pounding and lasting machines are mining, quarrying, road-making, shipbuilding and shoemaking establishments, locomotive and other work shops and airplane factories. This condition is also said to occur in telephone operators,⁸ but not in our observation of numerous operators.

Glass Fiber

Champeix¹¹ reports mechanical irritation from glass fiber. Manifestations consisted of cutaneous erythema with pruritus, blepharitis and rhinopharyngeal irritation. In the weaving of glass fiber, the dust is not so much harmful as annoying because of the almost incessant itching.

In the manufacture of camouflage nets,¹² cutaneous reactions to spun glass (fiber glass or glass wool) appeared in a group of women handling it. The reactions observed were itching, without demonstrable lesions, and folliculitis. Spun glass is composed of fine threads that float in the air like dust and adhere readily to the skin.

Asbestos Materials

Workers handling asbestos materials — especially amosite, a natural form of asbestos — develop painful warts or corns.¹³ Of 167 workers, 99 presented one or more lesions. Those affected feel a small, splinterlike foreign body in the tips of the fingers, extraction of which is usually unsuccessful. In less than two weeks, a small cornlike tumor appears at the site of injury. This lesion grows slowly and is tender to pressure. When cornification is pronounced, small corns appear on the fingertips and knuckles.

Klauder and Hardy¹⁴ report similar lesions in pipe coverers who handle asbestos with ungloved hands. Workers call this lesion an asbestos corn or wart. The lesion represents a foreign-body reaction to spicules of asbestos that penetrate the skin.

Chlorinated Hydrocarbons

The eruption caused by the chlorinated waxes — chlorinated naphthalene, diphenyl and diphenyl oxide — is called chloracne or cable rash. Differentiation of this eruption and that seen in ordinary acne vulgaris is done by obtaining a history of exposure to the hydrocarbon in question and by finding acneform lesions in areas behind the ears and on the nape of the neck, the buttocks, thighs, knees, abdomen and lower back. These sites are not involved in acne vulgaris.

In a navy yard, over 200 cases of chloracne were observed.¹⁵ The incidence of this rash has increased

because of the great acceleration of the shipbuilding program. Workers come in contact with water-proofed, fireproofed cable impregnated with chlorinated naphthalene, chlorinated diphenyl or chlorinated diphenyl oxide.

Folliculitis was caused by chlorinated hydrocarbons in 5 of a series of 1113 cases of cutaneous disease reported by Klauder¹⁶ in 1943. In an additional 1184 cases reported by Klauder and Hardy¹⁴ 3 cases were chloracne.

The lesions in chloracne are due to chloro compounds deposited as fine particles or condensations on the skin from fumes and solutions.¹⁷ Such compounds plug the follicular orifices and by their keratogenous action cause the formation of comedones. Yellow cysts develop as a result of mechanical plugging of the openings of the glands and the actual keratinization of their walls. Preventive measures in general are the proper selection of workers, cleanliness, the wearing of clean clothing and adequate ventilation. Workers with a tendency to seborrhea or acne should be excluded from this type of work, since they are as a rule more susceptible than others to acneform eruptions.

Cutting Oils

The cutting oils are the most frequent cause of dermatoses in factories engaged in the making and machining of metal parts. In the manufacture of the actual materials for airplanes, tanks, guns and vehicles this vexing problem confronts the industrial physician.

There are two large groups of cutting oils, the soluble and the insoluble. The former consists of a mixture of sulfonated mineral oil and soap containing resin, sulfonic acids and preservatives — phenol, creosol or nitrobenzene — when animal or vegetable fats are used in the oils. These oils are mixed with water and allowed to flow continuously over the material under operation. Their chief function is the cooling of the metal parts. The insoluble oils are mixtures of mineral, animal and vegetable oils, sulfur and chlorine. The last two chemicals enable deeper cuts to be made into the metal without harming the cutting tools. In the oils containing animal or vegetable oils, inhibitors such as phenolic amines are added to prevent rancidity.

Mineral oils cause defatting of the skin. The small amount of animal or vegetable oils present tends to counteract this effect. The cutting oils produce lesions of the skin owing to mechanical interference with or plugging of the pores. Dermatitis, both sensitization and nonsensitization, irritations, abrasions due to metal shivers in the oils and secondary infections are caused by cutting oils. For the sake of simplicity the skin manifestations of these oils are mentioned under this heading.

In a group of 450 cases of occupational dermatosis reported as to cause, 45 (8.5 per cent) were due to petroleum products.¹⁸ Thirty-six cases were of the

oil folliculitis type. There were 1 case each of generalized melanosis, localized melanosis, keratosis and epithelioma and 7 cases of nonsensitization dermatitis from cutting oils. Oil folliculitis was the most frequent form of dermatosis in workers exposed to lubricating oils and greases and was severe in most cases.

Klauder¹⁶ examined 128 men operating automatic screw machines and found comedones, small follicular, hornv papules, acnelike papules, pustules, pyoderma and scars resulting from destruction of the follicular orifices. In only 19 per cent of the workers were no lesions found. In another study of 50 cases of folliculoses,¹⁴ 42 were found to be caused by mineral oil in machine operators and men engaged in quenching metals. Two of these cases were complicated by cellulitis and lymphangitis.

Peck¹⁷ reports that dermatitis from cutting oils, especially those of the insoluble type, occurs more frequently than any other occupational skin disease. The lesions oftenest seen are folliculitis and comedones on the hairy portions of the arms and the anterior surfaces of the thighs.

Schwartz,^{18, 19} after making a survey of the various skin hazards in war industries, reports that cutting oils are frequent causes of dermatitis. They defat and irritate the skin and plug the pores. The sulfur, chlorine or rancid animal or vegetable fats in the oils are irritating. Phenols, creosols, nitrobenzene and other inhibitors present in the oils may sensitize the skin, and steel shivers in dirty oils often cut the skin.

Allergic eczemas are the least frequent types of cutting-oil dermatitis.

Some mineral oils have keratogenic properties and cause papillomas and warts. Schwartz¹⁸ found these lesions in 10 per cent of the workers, an exceedingly high percentage that does not correspond with the observation of others. Certain oils are carcinogenic, but fortunately the mineral oils of North America are low in the carcinogenic scale. Some cases of skin cancer, however, occur in the United States as the result of contact with mineral oil. There was 1 case of epithelioma in 45 cases of dermatosis due to petroleum products.¹⁸

Prevention consists essentially in reducing to a minimum the contact between workers and irritants. Machines should be kept free from grease and dirt by daily cleaning. Oil should not be allowed to accumulate on the floor. Guards should be attached to machines to prevent oil from splashing on workers. Adequate washing facilities and clean work clothes should be provided, and impervious sleeves and aprons should be worn. Klauder¹⁶ advises the use of two protective ointments, the first being

smear thickly over the entire forearm as a base for the second. These ointments are composed as follows:

FIRST OINTMENT		SECOND OINTMENT	
	gm		gm or cc
Zinc oxide	25	Ethyl cellulose	5
White petrolatum	25	Mastic	8
Kaolin	50	Castor oil	1
		Acetone (technical)	86

The second solution is applied with a small brush and dries, leaving a film that is repellent to both water and oil.

Abrasions, Cuts, Friction and Pressure

Abrasions, lacerations and fissures often occur throughout the fish industry, and subsequent infections are frequent and disabling.²⁰ Metal slivers in the cutting oils produce cuts of the skin.¹⁸

Stigmas peculiar to certain occupations are due to pressure, friction, repeated injuries and joint deformities. Ronchese²¹ enumerates the following trades with their stigmas. Stone chisellers have a characteristic large, soft, rubbery callus at the proximal end of the left little finger. Painters and paperhangers have an elongated callus in the center of each shin, owing to pressure of the rung of the ladder. Jewelers, engravers, ringmakers and stone setters show a characteristic large, heavy callus in the center of the right palm, produced by their most important tool, the plier. Mechanics, machinists and toolmakers as a rule have rough hands showing cuts and abrasions. The nails are worn down, the fingertips are often raw, and the palms are studded with metal slivers from handling and filing metal parts. Foundry workers and melters of metals show a vivid-red discoloration (erythema ab igne) of the forearm, which is continuously exposed to intense dry heat in the act of pulling metals from ovens. The shins of junk collectors, garbage men, truck drivers and railroad conductors show varying degrees of abrasions, cuts, scars and pigmentation. This condition is due to frequent trauma to the shins.

Perhaps the most important physical agent of this era from the point of view of health is radioactive material. Its effect on human tissue has merited and will continue to merit careful consideration. In a nonindustrial paper Dunlap²² presents an excellent review of the injuries resulting from roentgen rays and radioactive substances. Years ago industrial physicians learned the deleterious effects of the alpha and beta rays emanating from radium on the health of persons who swallowed or inhaled radioactive substances or took them into their bodies in other ways. Physicists have succeeded in rendering practically all the known elements temporarily radioactive by exposing them on a precursor to the enormous energies generated by the cyclotron. Thus a new industrial hazard is incurred by persons work-

ing with or near cyclotrons or their radioactive products.

The character of tissue damage appears to be identical with the injuries resulting from exposure to roentgen rays or radium. In the manufacture of roentgen-ray tubes there is an obvious hazard to employees for which in most factories there is adequate protection. Detection of flaws in metal castings and welds by roentgenograms and radium photography requires the use of enormous doses of radiation, from which serious effects result if there is no intelligent medical supervision. Insurers in Boston learned this several years ago when an efficiency expert introduced an x-ray machine to speed up a certain process, with resulting radio-dermatoses to workers exposed. The manufacturers of luminous dials have learned the terrible toll among their workers from inexperience in handling minute amounts of radioactive material. The manufacture and handling of radium applicators and needles involve exposure not only to radiations but also to radon gas in the atmosphere and to the chance in halation or ingestion of particles of radium. The mining and handling of radioactive ores should be closely supervised. Although no medical difficulties have been encountered among the miners of pitchblende, the chief source of radium, workers in the cobalt mines of Germany suffered for centuries from an obscure disease of the lungs, recently identified as cancer, that was probably due to inhaled radon gas. Chemists who have worked with radium and related compounds have suffered from burns and anemias. Human curiosity and careless supervision of roentgen-ray equipment, especially the fluoroscope, may be disastrous. A number of workmen in a large industrial plant on the West Coast were seriously burned in a recent series of laymen's experiments conducted with a fluoroscopic machine in the first-aid room.²²

FLOWERING PLANTS AND THEIR PRODUCTS

Woods and Weeds

Piorkowski,²³ observing that dermatitis is frequent among workers handling tropical woods, reported 5 cases in Indians handling mvule wood, which is similar to teak and oak in its uses. The clinical picture was that of an acute dermatitis venenata covering the exposed parts of the face, neck, forearms and hands and causing severe itching. The eyelids were swollen. In 1 case catarrhal conjunctivitis and rhinitis were present. In 4 cases the onset was sudden and the attack lasted for one or two weeks, in another it lasted for six months. The eruption developed subsequently and consisted of chronic eczematous changes, marked pruritus and lichenification. The chemical agents responsible are the alkaloids or nonsaturated resinous acids.

Howell²⁴ in a recent article on contact dermatitis reports that in the Southwest an eczematous contact dermatitis from sensitization to vegetation is a

frequent occurrence. The condition is an occupational hazard among ranchers, farmers and workers in the oil fields. Howell reported 35 patients who were sensitive to weeds — some to several and others to only one. This was brought out by patch tests with the oleoresins of forty-five different weeds.

Extracts and Resins

Cashew-nut-shell oil. The oil of the cashew nut shell is obtained either by roasting the shells, the general practice in India, or by solvent extraction, which is said to produce a much higher yield of oil. The oil is a mixture of 90 per cent monohydric phenol (anacardic acid) and 10 per cent polyhydric phenol (cardol). The cardol fraction is believed to contain the major irritant properties of this oil and is related chemically to urushiol, the irritant principle of poison ivy. Cashew-nut-shell oil has been proved to be a primary irritant and a sensitizer.²⁵ Two patients had to be hospitalized as a result of patch testing with this substance. The oil would be invaluable in industry except for these deleterious properties.

An investigation²⁶ of the manufacture and use of this liquid was conducted when occupational dermatitis due to resinous varnish made from cashew-nut-shell oil and formaldehyde occurred among many workers handling electric components insulated with this varnish. One plant visited had been using cashew-nut-shell oil for nineteen years, manufacturing a variety of resins including insulating varnish, dusts for brake linings, molding powders and millable rubbery compounds. These materials represent products of cashew-nut-shell oil and other chemicals in various stages of polymerization and condensation or cure. In this plant 4 of every 10 new workers handling the raw oil develop dermatitis, and one quarter of the attacks are severe. Patch tests with this oil on 15 subjects showed marked reactions at the end of twenty-four hours in all subjects, which proves that it is a primary skin irritant. Cured varnish caused a positive patch-test reaction in only 1 case.

Lockey²⁷ reports contact dermatitis as developing in 9 men who for some time had been using so-called "H varnish E 107," which contains cashew-nut-shell liquid as one of its main bases. Patch tests revealed that all these men were sensitive to the oil, 7 reacted to the varnish from the barrel that was being used at the time the dermatitis appeared, whereas none reacted to varnish used previously. It is probable that the oil had not been properly broken down in the manufacturing process.

Resins. Over twenty-six hundred objects used in this country are made of resins.²⁸ The phenol formaldehyde and urea formaldehyde resins account for many cases of contact dermatitis during the process of their manufacture. Dermatitis appeared in 78 of 150 workers engaged in making tubes for launching rocket bombs from airplanes, these tubes

were made from paper glued together with a low-polymerized phenol formaldehyde resin.²⁹

Cranch³⁰ states that the outstanding source of trouble in the use of plastics is local — that is, dermatitis. The finished products made from plastics are seldom irritants, and in only a few cases do they cause sensitization with resulting dermatitis.

Hall,⁷ in analyzing occupational dermatitis among aircraft workers, found that those using zinc primer reacted to zinc chromate or to the resins in the primer (phenol formaldehyde, a natural resin and a phtholic anhydride) or to both. Of those who reacted to the primer, 13 per cent were sensitive to one or more of the resins but not to the zinc chromate, and 15 per cent were sensitive to one or more of the resins and also to zinc chromate.

The dermatitis due to resins was uniform in its characteristics. The eyelids were affected in all cases, and the side of the upper two thirds of the neck and the cubital fossas in the great majority. The hand and fingers were affected in only 1 case, and the wrists and forearms in only 6. The average duration of exposure before onset of symptoms was seven months — less than that for zinc chromate. In 3 cases, however, the average duration was less than a week.

Lemon-grass oil. Mendelsohn³¹ reports dermatitis in 8 machinists, carpenters and riggers who worked for three weeks on a ship recently arrived from India. Part of the cargo comprised tanks of lemon-grass oil, some of which was spilled. The cutaneous lesions appeared six to eighteen days after this work. The eruption consisted of discrete and confluent erythematous patches of various sizes, some slightly vesicular. The lesions were on the face, on the flexor aspects of the lower two thirds of the forearms and about the ankles. Three men had edema of the eyelids, and 1 also had considerable dermatitis of the penis, scrotum and upper part of the thighs. Two men reported that members of their families had similar rashes, evidently following contact with their contaminated work clothes. Four workers were patch tested with pieces of pine wood soaked in lemon-grass oil, and all showed strongly positive reactions. Lemon-grass oil has many uses, it is employed in the manufacture of perfume and ionene and as an adulterant for lemon oil.

Fruits and vegetables. In the picking, packing and canning of fruits, various forms of cutaneous irritation are encountered.³² In the citrus fruit industry, dermatitis is caused by the irritant oil in the rind of lemons, oranges, limes and grapefruit. Among the pickers of such fruits, dermatitis is produced by the thorns on citrus trees and by the insecticides and fumigicides sprayed on them. Paronychia occurs among canners of these fruits. Pineapple peelers develop dermatitis from the sharp spears on the fruit, and the high sugar content of

pineapples also causes dermatitis. The sharp fuzz on peaches is irritating to pickers and canners, and the sugar in the juice is also irritating to the skin.

Dierker³³ reports the results of an investigation of dermatitis occurring in a small plant producing marmalades and jellies. No skin irritation was encountered among the workers until a load of Seville oranges was converted into marmalade. The oranges were washed and dried, the skins were removed, and the fruit was cut up. In this operation 5 of 10 workers developed diffuse erythema of the dorsum of the hands and wrists and the webs of the fingers. Patch tests on 8 normal subjects with extracts of the orange skins as well as juice from the fruit elicited no reaction. The workers with dermatitis were not tested. The patch tests, however, gave evidence that no primary irritant was the cause of the dermatitis. It was thought that the high acidity of this species of orange, together with the continuous wetting of the hands, produced the dermatitis. The use of a protective cream against acid, dipping the hands in a weak solution of sodium bicarbonate and the wearing of gloves prevented further trouble.

Peck³⁴ reported dermatitis arising from the dehydration of potatoes. He inspected six plants engaged in this process, only one of which used lye in the peeling process. The potatoes were washed, precooked, immersed in a 10 per cent lye solution and peeled by friction in a rotating drum. The final washing removed all traces of lye. In the other five plants the potatoes were precooked and peeled by rough rubber rolls, no lye being used. After peeling the potatoes were brought to the trimming tables by moving belts, where workers trimmed off the remnants of the peel with special knives, their hands were constantly wet with water and potato juice in this operation. Dermatitis of the hands, which occurred in 24 women workers, started in the hand holding the potato in the trimming operation, it consisted of redness, scaling and sometimes vesicles in the web spaces, resembling *erosio interdigitalis blastomycetica* as the condition progressed. Patch tests with slices of potato, cooked and uncooked, on 12 workers and 5 controls were negative.

This dermatitis is due to long exposure to water and potato juice, which results in maceration of the skin. Workers whose hands are thus constantly wet eventually develop dermatitis and show interdigital maceration and redness suggestive of *erosio interdigitalis blastomycetica*. Patch tests are unnecessary, for no such test can reproduce the occupational exposure. The workers affected include dishwashers, salad makers, vegetable salesmen, cooks, peelers and canners of vegetables and young housewives—by far the largest group encountered in the private practice of one of us (JGD).

Dermatitis occurred in 17 women who worked with carrots.³⁵ The cutaneous eruption appeared on the palms, the thenar and hypothenar eminences, the dorsum of the hands and forearms and in some cases even the neck, face and eyelids. The incubation period was generally from seven to ten days but sometimes lasted for several months. When workers were removed from contact with either cooked or uncooked carrots, the dermatitis cleared up. Patch tests with carrots, cooked and uncooked, indicated that they were definitely the cause of the eruption.

Thirteen women handling partially decayed parsnips for three or four weeks developed dermatitis.³⁶ When the parsnips were cut, the juice ran down the back of the left hand and sometimes down the knife to the right hand. On exposure to the sun, redness, swelling and then pigmentation developed at these sites. Six other women similarly exposed were not affected.

(To be concluded)

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND SIXTY-FIFTH ANNIVERSARY

May 21, 22, and 23, 1946

THE one hundred and sixty-fifth anniversary of the Massachusetts Medical Society was observed in Boston on Tuesday, Wednesday and Thursday, May 21, 22 and 23, 1946, at the Hotel Statler

Seventeen hundred and fifty physicians were registered

TUESDAY, MAY 21

The first scientific session began at 2:00 p m At 5:00 p m the supervising censors met in Parlor D The Cotting Supper was served to 185 councilors in Parlors A and B The annual meeting of the Council was held in the Georgian Room at 7:00 p m There were 191 councilors in attendance

WEDNESDAY, MAY 22

The second scientific session was held under the joint co-chairmanship of Dr W Jason Mixer and Dr C J E Kichham The attendance varied from 500 to 600

The one hundred and sixty-fifth annual meeting of the Society was held at 11:00 a m in the Georgian Room Dr Reginald Fitz presided The attendance was 500 Dr Fitz spoke at length on "The State of the Society" The Annual Oration, entitled "Gastric Surgery," was delivered by Dr Frank H Lahey The annual luncheon was served in Parlors A, B and C to 219 fellows

The third scientific session was held in the Georgian Room from 2:00 to 4:00 p m under the co-chairmanship of Dr Elmer S Bagnall and Dr John Fallon The attendance was 600 The Shattuck Lecture was delivered at 4:00 p m by Dr John B Youmans, whose subject was "Nutrition and the War" (This lecture appeared in the June 13 issue of the *Journal*)

The annual dinner was held in the Georgian Room at 7:00 p m with 525 in attendance The principal speakers were Dr Roger I Lee, president of the American Medical Association, and Dr Elmer S Bagnall, former president of the Massachusetts Medical Society

THURSDAY, MAY 23

A general scientific session began at 9:00 a m and continued until noon under the co-chairmanship of Dr Archibald McK Fraser and Dr Arthur J Gorman The attendance was between 550 and 600

From noon until 2:00 p m a series of section meetings and luncheons was held The Section of Medicine, under the chairmanship of Dr Albert A Hornor, met in Parlor B Fifty-one sat down to luncheon The Section of Surgery, under the chairmanship of Dr Charles F Twomey, met in the Salle Moderne The attendance was 133 The Section of Pediatrics, under the chairmanship of Dr Floyd R. Smith, met at the Junior League, Zero Marlborough Street The attendance was 55 The Section of Obstetrics and Gynecology met in Parlor A, under the chairmanship of Dr Arthur F G Edgelow The attendance was 52 The Section of Radiology, under the chairmanship of Dr George Levene, met in Room 400 The attendance was 28 The Section of Physical Medicine, under the chairmanship of Dr Arthur L Watkins, met in Parlors D and E The attendance was 12 The Section of Dermatology, under the chairmanship of Dr Bernard Appel, met in the Hancock Room The attendance was 38 The Section of Anesthesiology, under the chairmanship of Dr Sidney C Wiggan, met in Parlor C The attendance was 29

From 2:00 to 5:00 p.m a general scientific session was held in the Georgian Room under the co-chairmanship of Dr Frank R Ober and Dr Harry Blotner The attendance was 600

There were seventeen scientific exhibits and eighty-four technical exhibits

The motion pictures, as usual, attracted a large number

The special list of officers, standing and special committees, councilors, censors, admissions and deaths are appended

MICHAEL A TIGHE, *Secretary*

ANNUAL MEETING OF THE SOCIETY

The one hundred and sixty-fifth annual meeting of the Massachusetts Medical Society was called to order by the president, Dr. Reginald Fitz, in the Georgian Room of the Hotel Statler, Boston, at 11:00 a. m., May 22, 1946. There were approximately 500 Fellows present.

The Secretary submitted the record of the last annual meeting held on May 23, 1944, as published in the *New England Journal of Medicine*, issue of August 3, 1944. It was moved and seconded that the record be adopted. It was so ordered by vote of the fellows.

The Secretary reported that the membership of the Massachusetts Medical Society, as of May 23, 1945, was 5786 and as of May 22, 1946, 5989. He said that 85 fellows had died, 16 had resigned and 6 had been deprived of membership. He added that 302 new fellows had been admitted and that 8 had been reinstated. It was regularly moved and seconded that the Secretary's report be accepted.

It was so ordered by vote of the fellows.

At the request of the President, the Vice-President, Dr. W. Jason Mixter, assumed the chair. Dr. Mixter spoke as follows:

Members of the Society, I should like to take a short moment to make a personal report on the activities of your president during the past year. You will find in his report that the condition of the Society is healthy. I am sure that one of the major reasons for this condition is the fact that Dr. Fitz has given lavishly of his time and energy to the business of the Society. He has used tact where tact was needed. He has used the authority of his office for the benefit of the Society where it was needed, and I feel that the Society owes a very large vote of thanks to Dr. Fitz for his activities as our president. Mr. President, I ask you to give your report on "The State of the Society."

Dr. Fitz responded as follows:

For the third time in the last hundred years the Society, on the occasion of its annual meeting, is in a period of readjustment following a great war.

In 1865, the finish of the War between the States was so close that the fellows scarcely as yet realized the full impact of peace. This meeting was poorly attended—in part because of the disturbed state of the Nation and in part because the American Medical Association was to assemble in Boston during the following week. There was no annual dinner, nor did the scientific program lay any great emphasis on war medicine. It is interesting, however, that the most debated topic under discussion by the American Medical Association dealt with specialists: what a specialist was, and what he was supposed to do.

At the annual meeting in 1919, military medicine received much more consideration. Nearly a third of the doctors in Massachusetts had experienced active military service, they seemed eager to resume their civilian occupations as promptly as they could but were equally willing to hear what the war had added to medical knowledge. The *Proceedings of the Council*, on the other hand, do not suggest that any very vital problems had developed, and indeed, except for one instance, the entire meeting was largely devoid of extraordinary contributions. It was at the annual dinner that Dr. Samuel B. Woodward, who was president, presented ideas not often mentioned. These ripened slowly with time and still promise important results. He said that all fellows should take a more active interest than heretofore in legislative matters and should have no reluctance in stating their opinions at the State House or anywhere else on matters concerning the health and welfare of their fellow citizens.

The past year has been an eventful one. As in 1919, approximately a third of our physicians have recently experienced active military service, and as in 1865, the matter of specialization is of vital interest.

A preview, obtained by questionnaires from the American Medical Association, suggested that a new type of practice might presently become manifest. The men in service wrote that they hoped, on discharge, for an urban type of practice rather than for a general practice in rural districts and that they looked forward to opportunities for postgraduate education with the idea of becoming specialists or of working in well organized groups. The Society realized these trends and, through the Postwar Planning Committee, arranged for appropriate steps to assist in their development, should these be necessary.

Our work in postgraduate education is an important milestone. By using available facilities all over the Commonwealth, we have administered, successfully, a variety of postgraduate courses, which have proved both popular and refreshing. More than a thousand doctors have had opportunity to bring themselves up to date on current medical ideas through expertly delivered lectures. In the words of the first Dr. John Warren, the result is that the Society has gone farther than ever before, for the benefit of its fellows, "to promote medical and surgical knowledge by encouraging a free intercourse with the Gentlemen of the Faculty."

The Society has watched the return of its medical officers with care as well as with pride. Apparently the majority of our veterans are as eager as were their older brothers to resume civilian work where they left it and as promptly as they could, up to the present time, they have made no significant attempt either to overspecialize or to overexpand group practices. To be sure, many young veterans are hoping to complete the program of training on which they had embarked before they entered military service. For these men, especially, the Bureau of Clinical Information fills a useful function. Opportunities for the supervised, long-continued type of hospital training demanded by specialty boards are, by necessity, limited. The Bureau of Clinical Information has kept track of such opportunities as there are, and the Postwar Planning Committee has endeavored to create new ones locally. A number of veterans, however, have been disappointed by their inability to find at once exactly the residencies that they hoped would be available. All that can be said is that the machinery of the Society is working to help such men as best it can.

The Postwar Loan Fund represents another attempt by the Society to assist returning veterans. The problems that face a man who has been out of civilian circulation for a few years are bewildering, not only in matters of education but also in the more earthy ones of finding a house in which to live or an office in which to practice or equipment with which to work. For these latter details, the Postwar Loan Fund is of assistance at least it may provide a much-needed sense of financial security.

Our executive work has continued to go forward through usual channels. As Dr. Lee pointed out two years ago, the Society operates through committees. During the past year, twenty-seven committees have functioned industriously on our behalf. It is the President's privilege to be present at all committee meetings that he desires to attend, and thereby he is given unequalled opportunity to keep abreast of the Society's activities.

Most of these committees have functioned with zeal far beyond the ordinary call of duty. I have already mentioned the educational accomplishments of the Postwar Planning Committee. This committee, through a subcommittee established to work in co-operation with subcommittees from the committees on Legislation and Public Relations, also struggled with a hydra that made its appearance at the end of World War I.

At the annual meeting in 1919, there was talk of the physical imperfections in the youth of America that had become manifest through examinations for the draft. This general subject gradually attained national popularity through one or another of its many heads until finally President Truman's National Health Program of 1946 emerged. The opinion of the Society on a matter so important to the nation was crystallized by these subcommittees, by their parent committees and finally by the Council, in the form of a short pamphlet. Herein the Massachusetts Medical

society offers certain basic principles to govern proper medical-care plans and expresses its views concerning national legislation now pending. This is an important document, interesting, chiefly, because it sets forth basic principles concerning the care of sick people to which the majority of fellows wish to subscribe, and interesting, also, because it shows so clearly the Society's philosophy. We wish everyone to have every known essential preventive, diagnostic and curative medical service of high quality. We believe that this can be best attained by a gradual process of evolution rather than by sudden revolution. We believe that it is the responsibility of persons who are able to do so to procure for themselves many phases of medical care by direct payment or by voluntary insurance against their costs. And finally, we continue to cherish an old ideal to receive the best kind of medical care we are convinced that every patient must have the right to select the physician or hospital to which he chooses to entrust the care of his health.

The activities of the Committee on Legislation are perennial. The Society has come a long way since Dr Woodward reminded us of our obligations as citizens. Fellows are less diffident than they used to be at hearings or indeed at meeting legislators as men to men. Several district societies have entertained their representatives or senators at dinner—an important method of breaking down existing barriers, members of the Great and General Court prove agreeable dinner companions, appearing fully as eager as we are to improve the health and welfare of our citizens and willing to hear our views.

The Committee on Legislation has experimented with a new method of organization. During the past year it has functioned through an executive committee and through subcommittees. In this manner each member of the committee has been kept informed of legislative matters in general and each subcommittee has worked intensively on such bills as were assigned it. One subcommittee, for example, studied, with particular care, antivivisection bills, another bills concerned with hospital staff appointments, and a third, the chiropractic bill. The Executive Committee has integrated the work of its subcommittees with the work of the parent committee, drawing heavily on Mr Charles Dunn for legal and technical advice. This method of organization seems reasonable, promises to yield good results and warrants further exploration.

Several months ago, Major General Paul R. Hawley requested the Society to appoint a committee to confer with his office about the medical care of veterans. The Council authorized the appointment of such a committee, which in turn worked most industriously. As a result it is hoped that certain veterans may be free, in case of need, to employ civilian physicians and hospitals of their own choice in Massachusetts. Their hospital expenses will be met through the Blue Cross as agent, and their professional bills will be met through the Blue Shield as agent, according to a fee schedule established to cover almost all professional services that can be offered. The construction of so comprehensive a fee table proved a difficult, time-consuming task, requiring the welding together of many different opinions from various groups of physicians, in its final form it represents, to a high degree, conscientious and painstaking effort.

At its stated meeting in October, the Council voted to blaze a new trail. The committees on Legislation, Postwar planning and Public Relations submitted a joint resolution advocating the creation of a new position in the Society—that of director of medical information and education. The need for a full-time worker in our executive offices had become increasingly apparent for several years, although the definition of the exact duties of such a person was more difficult. The Council supported the resolution offered by these committees and voted to appoint a special committee to nominate a suitable candidate for the new post. This committee as yet has made no nomination, preferring to act slowly on a matter of such importance, the establishment of this position is certain to have far-reaching results.

At the stated meeting in February, the Council made another departure from old ways. It advocated a plan whereby certain licensed physicians in Massachusetts who were graduates of unrecognized medical schools might obtain hospital privileges. This action represents a broad-

minded attitude in the treatment of an old sore point. Everyone knows that Massachusetts, in the past, has licensed a number of physicians who graduated from unrecognized medical schools, and that by last year's legislative action their future source of supply was jugulated. On the other hand, such doctors, already licensed, will continue to practice and are the family physicians of many patients. Dr H. Quimby Gallupe, of Middlesex South, to aid these men and their patients, presented an ingenious plan by which courtesy-staff hospital privileges under carefully supervised regulations could be made more generally available to them. The Council adopted the plan, and the Committee to Meet with the Massachusetts Hospital Association has been assigned the duty of furthering it. Already a series of meetings with hospital representatives has commenced at which the details of the plan will be discussed around a small table with the informality that is possible when small groups are involved. This is an important step. If both hospitals and fellows co-operate to activate this plan, the Society will be able to take credit for having promoted a liberal and unselfish program primarily designed for public benefit but also having substantial educational value.

Twenty-five years ago, the *New England Journal of Medicine* became owned by the Society and subsequently has been published by it. We have been wise in our choice of editors. Dr Walter P. Bowers laid the foundation for the *Journal's* present success and Dr Robert N. Nye has continued to carry forward his aims. During 1945, about 18,000 readers received the *Journal* each week, and the enthusiasm with which our published articles and editorials have been received all over the world is indeed flattering.

I have selected these few features in the Society's most recent history to emphasize how, little by little, our influence and interests expand. In spite of so much exertion our physical condition is satisfactory. Our membership increases steadily, our finances are in good order, and our spirit is that of ardent youth tempered by our recorded age.

Each president, as he discusses the state of the Society at the annual meeting, by necessity renders his report with mixed feelings of pride and humility. For all his days he must remain proud that his colleagues have paid him the compliment of allowing him to occupy the highest office in the Society for a year. On the other hand, he is humble because he realizes how small a part he has played even for those few months, in carrying on the efforts of so large an organization as the Society has grown to be.

The district societies, the Council, the committees with their devoted chairmen, Robert N. Nye, of the *Journal*, Robert St. B. Boyd, the executive secretary, Miss Cowles, tireless in keeping our records straight, Eliot Huhhard, Jr., ever watchful of our purse and, above all, Michael Tighe, tolerant and wise, are our flag-bearers. They are the ones who keep our ideals viable and continue to make Dr Jacob Bigelow's words of a century ago so timely: "I give you, gentlemen, the Massachusetts Medical Society, old but not infirm, numerous but not divided. May it long continue to be what hitherto it always has been the protection and pride of those who are worthy to be its members."

The President resumed the Chair. At the direction of the President, the Secretary read the following amendment to the by-laws:

The by-laws of the Massachusetts Medical Society are hereby amended by adding a new chapter, to be known as Chapter X. The chapter shall read as follows:

Any provision or provisions of these by-laws may be temporarily waived, provided such waiver is not in conflict with the laws of the Commonwealth, provided the provision or provisions sought to be waived are clearly designated, provided the period during which such waived provision or provisions are to continue be definitely stated, provided notice of the proposed waiver accompany the call of the annual meeting and provided the members present at such an annual meeting unanimously consent.

The President explained that this amendment was legally before the Society for action. It had been

approved by the Council and had accompanied the notice of the annual meeting. Its intent, he continued, was to make the by-laws more flexible. The Secretary moved the adoption of the amendment. This motion was seconded and was so ordered by vote of the fellows.

Dr Thomas A Foster, delegate from the Maine Medical Association, was introduced. He responded as follows:

Mr President and members of the Massachusetts Medical Society, the Maine Medical Association and the Massachusetts Medical Society have had a long and friendly relation, the Maine Medical Association being born in 1820, when Maine became separated from the Commonwealth of Massachusetts. During that time we have sent many delegates to the annual meetings of the Massachusetts Medical Society.

With the permission of your president I should like to read some extracts from the report of a delegate to a meeting of the Massachusetts Medical Society, Thomas Albert Foster, of Portland, in 1871:

At twelve noon a meeting was holden in Lowell Institute at which several essays were read by young men who, from the character of their papers, I judge, will make their mark in the profession of medicine in that city. One of them, Dr Fitz I think they called him, I was told had recently returned from Germany where he had been spending some time under the instruction of Professor Burkhardt. His essay was on tuberculosis and was an able declaration.

The delegate speaks at length of other parts of the meeting and made a conclusion that I am not altogether sure is courteous.

As a whole, I think the Massachusetts Medical Society, although having among its members many of the ablest physicians and surgeons of the Country, is very far behind our own association in point of work. As good as the papers were, the subjects upon which they were written were by no means exhausted by their authors and still there was no discussion of any interest upon any of them. I am sure I can return to the Maine Medical

Association and find they still have the ablest physicians and surgeons and their papers are thoroughly prepared and exhausted. The discussion was enlightening.

The President read the list of officers elected by the Council on May 21, 1946.

Dr Fitz then introduced the incoming president, Dr Dwight O'Hara. Dr O'Hara responded as follows:

President Fitz and fellows of the Society, I told the Council last night that my main endeavor will be to continue as nearly as I can to following in the performance and pattern of the administration that Dr Fitz has set up during the past year. I know that I shall not attain his efficiency, but I shall endeavor to do so and I shall count on your support therein. Thank you.

Dr Fitz then introduced Dr Edward P Bagge, the president-elect. Dr Bagge responded as follows:

Mr President and fellows, this is indeed a historic occasion. I believe that I am the first pediatrician who has been put in line for the presidency. I shall try to live up to all the good beginnings that pediatricians are trained in and let the chips fall where they may. I hope that I shall not disappoint the electors.

At this point in the meeting the President introduced Dr Frank H Lahey, who presented the Annual Oration. His subject was "Gastric Surgery." The address was brilliantly given. It held the close attention of the audience through its entire delivery. (The oration appeared in the June 20 issue of the *Journal*.)

Dr Fitz declared the one hundred and sixty-fifth annual meeting of the Massachusetts Medical Society adjourned at 1 00 p m.

MICHAEL A TIGHE, Secretary

APPENDIX

OFFICERS FOR 1946-1947

PRESIDENT Dwight O'Hara, Waltham Office, Boston (15), 416 Huntington Avenue
 PRESIDENT-ELECT Edward P Bagge, Holyoke, 207 Elm Street
 VICE-PRESIDENT Isaac S F Dodd, Pittsfield, 34 Fenn Street
 SECRETARY Michael A Tighe, Lowell Office, Boston (15), 8 Fenway
 TREASURER Eliot Hubbard, Jr, Cambridge, 29 Highland Street
 ASSISTANT TREASURER Norman A Welch, West Roxbury Office, Boston (15), 520 Commonwealth Avenue
 ORATOR Leland S McKittick, Boston (16), 205 Beacon Street

COMMITTEES ELECTED BY THE DISTRICTS

Executive Committee of the Council — Established 1941 (members *ex-officio* and one councilor and alternate elected by the councilors of each district medical society)
 PRESIDENT Dwight O'Hara, Waltham Office, Boston (15), 416 Huntington Avenue.
 PRESIDENT-ELECT Edward P Bagge, Holyoke, 207 Elm Street
 VICE-PRESIDENT Isaac S F Dodd, Pittsfield, 34 Fenn Street.
 SECRETARY Michael A Tighe, Lowell Office, Boston (15), 8 Fenway
 TREASURER Eliot Hubbard, Jr, Cambridge, 29 Highland Street.

Term Expires 1947

BERKSHIRE Isaac S F Dodd, Pittsfield, 34 Fenn Street. (Alternate Clement F Kernan, Pittsfield, 184 North Street)

FRANKLIN John E Moran, Greenfield, 31 Federal Street. (Alternate Frank A Millett, Greenfield, 40 High Street.)
 HAMPSHIRE William A R Chapin, Springfield, 121 Chestnut Street. (Alternate Archibald J Douglas, Westfield, 3 Court Street.)
 MIDDLESEX NORTH William F Ryan, Lowell, 219 Centre Street. (Alternate Walter L Twarog, Lowell, 11 Durant Street.)
 NORFOLK Charles J Kickham, Brookline Office, Boston (15), 508 Commonwealth Avenue. (Alternate Henry M Emmons, Boston, 354 Commonwealth Avenue.)
 WORCESTER NORTH C Bertram Gay, Fitchburg, 62 Day Street. (Alternate John J Curley, Leominster, 89 West Street.)

Term Expires 1948

ESSEX SOUTH Walter G Phippen, Salem, 31 Chestnut Street. (Alternate None.)
 HAMPSHIRE Henry A Tadgell, Belchertown, Belchertown State School. (Alternate Lawrence N Durgin, Amherst, 66 Amity Street.)
 MIDDLESEX SOUTH Harold G Giddings, Newton Centre Office, Boston (16), 270 Commonwealth Avenue. (Alternate Arthur M Jackson, Everett [49], 512 Broadway.)
 NORFOLK SOUTH Daniel B Reardon, Quincy (69), 1186 Hancock Street. (Alternate Nahum R Pillsbury, South Braintree [85], Norfolk County Hospital.)
 SUFFOLK Alexander J A Campbell, Boston (15), 520 Commonwealth Avenue. (Alternate Howard F Root, Boston [15], 81 Bay State Road.)

WORCESTER Bancroft C Wheeler, Worcester, 27 Elm Street
(Alternate Franklyn P Bousquet, Worcester, 390 Main
Street [interim appointment])

Term Expires 1949

BARNSTABLE Paul M Butterfield, Harwich (Alternate
Paul P Henson, Hyannis, 149 Main Street)

BRISTOL NORTH Joseph L Murphy, Taunton, 23 Cedar
Street. (Alternate Curtus B Kingsbury, Taunton, 63
Prospect Street)

BRISTOL SOUTH Richard B Butler, Fall River, 278 North
Main Street (Alternate Curtus C Tripp, New Bedford,
416 County Street)

ESSEX NORTH Rolf C Norris, Methuen, 247 Broadway
(Alternate George J Connor, Haverhill, 81 Merrimack
Street)

MIDDLESEX EAST Kenneth L MacLachan, Melrose, 1 Belle-
vue Avenue (Alternate Justin L Anderson, Reading,
53 Woburn Street)

PLYMOUTH George A Moore, Brockton, 167 Newbury Street
(Alternate Alfred L Duncombe, Brockton, 38 Winthrop
Street.)

Committee on Public Relations — Established 1931 (one
councilor elected yearly by each district medical society,
the president and president-elect of the Society are
chairman and vice-chairman, respectively, and the vice-
president and secretary of the Society are members
ex-officio)

BARNSTABLE Paul P Henson, Hyannis, 149 Main Street

BERKSHIRE Patrick J Sullivan, Dalton, 471 Main Street

BRISTOL NORTH Milton E. Johnson, Attleboro, 33 Bank
Street.

BRISTOL SOUTH Harold E Perry, New Bedford, 159 Cottage
Street.

ESSEX NORTH Harold R Kurth, Lawrence, 57 Jackson
Street.

ESSEX SOUTH Loring Grimes, Swampscott, 84 Humphrey
Street

FRANKLIN Frank A Millett, Greenfield, 40 High Street

HAMPDEN Patrick E Gear, Holyoke, 188 Chestnut Street

HAMPSHIRE Joseph R Hobbs, Williamshurg, Main Street

MIDDLESEX EAST Milton J Quinn, Winchester, 44 Church
Street.

MIDDLESEX NORTH Daniel J Ellison, Lowell, 8 Merrimack
Street

MIDDLESEX SOUTH Gordon M. Morrison, Wahan Office,
Boston (15), 520 Commonwealth Avenue

NORFOLK Dean S Luce, Canton, 553 Washington Street

NORFOLK SOUTH Henry A. Robinson, Hingham, 205 North
Street.

PLYMOUTH Charles D McCann, Brockton, 12 Cottage Street.
SUFFOLK Albert A Hornor, Boston (15), 319 Longwood
Avenue.

WORCESTER Nicholas S Scarcello, Worcester, 1 Sheldon
Street.

WORCESTER NORTH James V McHugh, Leominster, 55 West
Street.

Subcommittees of the Committee on Public Relations

LABOR AND INDUSTRY — Established 1945

Daniel B Reardon (Norfolk South), *chairman*, George
J Connor, Essex North, Daniel J Ellison, Middle-
sex North, John Fallon, Worcester, and Michael A.
Tighe, Middlesex North

**COMMITTEE TO MEET WITH THE MEDICAL ADVISORY COM-
MITTEE OF THE INDUSTRIAL ACCIDENT BOARD** —
Established 1942

Daniel J Ellison (Middlesex North), *chairman*, Gordon
M Morrison, Middlesex South, and David D
Scannell, Norfolk

POSTPAYMENT MEDICAL CARE — Established 1942

Daniel J Ellison (Middlesex North), *chairman*, Michael
F Barrett, Plymouth, James H Brewster, Bristol
North, James T Brosnan, Worcester, Lucien R
Chaput, Essex North, Charles F Fasco, Berkshire,
Patrick E Gear, Hampden, Loring Grimes, Essex
South, Francis T Janitzen, Suffolk, Egon E Katt-
winkel, Middlesex South, Howard M Kemp, Frank-
lin, William B LeBrecht, Worcester North, Wilfred

L McKenzie, Middlesex East, Harold E Perry,
Bristol South, Daniel B Reardon, Norfolk South,
Harold F Rowley, Barnstable, Elmer E Thomas,
Hampshire (interim appointment) and Norman A
Welch, Norfolk

TAX-SUPPORTED MEDICAL CARE — Established 1940

Thomas Hunter (Worcester), *chairman* (interim appoint-
ment), Frederick S Hopkins, Hampden, Albert A
Hornor, Suffolk, William J Pelleter, Franklin, and
Frank W Snow, Essex North

Committee on Legislation — Established 1942 (one coun-
cilor elected yearly by each district medical society)

BARNSTABLE To be appointed

BERKSHIRE John Hughes, Pittsfield, 74 North Street

BRISTOL NORTH Curtus B Kingsbury, Taunton, 63 Prospect
Street

BRISTOL SOUTH Curtus C Tripp, New Bedford, 416 County
Street

ESSEX NORTH Nicandro F DeCesare, Methuen Office,
Lawrence, 57 Jackson Street

ESSEX SOUTH To be appointed

FRANKLIN Arthur W Hayes, Greenfield, 78 Federal Street

HAMPDEN Arthur H Riordan, Indian Orchard, 147 Oak
Street

HAMPSHIRE Lawrence N Durgin, Amherst, 66 Amity Street.

MIDDLESEX EAST John M Wilcox, Woburn, 6 Bennett
Street

MIDDLESEX NORTH Archibald R Gardner, Lowell, 16
Shattuck Street

MIDDLESEX SOUTH Kenneth J Tillotson, Belmont. Office,
Waverly, McLean Hospital

NORFOLK To be appointed

NORFOLK SOUTH David L Belding, Hingham Office, Boston
(18), 80 East Concord Street

PLYMOUTH Alfred L Duncombe, Brockton, 38 Winthrop
Street

SUFFOLK William E Browne, Boston (15), 587 Beacon Street

WORCESTER George R Dunlop, Worcester, 53 Massachu-
setts Avenue

WORCESTER NORTH John J Curley, Leominster, 89 West
Street

Subcommittee of the Committee on Legislation

NATIONAL LEGISLATION — Established 1946

Elmer S Bagnall, (Essex North), *chairman*, Reginald
Fitz, Suffolk, James C McCann, Worcester, and
Michael A Tighe, Middlesex North

Committee on Nominations — Established 1874 (one coun-
cilor and alternate elected yearly by each district medical
society)

BARNSTABLE Paul M Butterfield, Harwich (Alternate
Paul P Henson, Hyannis, 149 Main Street)

BERKSHIRE Patrick J Sullivan, Dalton, 471 Main Street.
(Alternate John Hughes, Pittsfield 78 North Street)

BRISTOL NORTH Joseph L Murphy, Taunton, 23 Cedar
Street. (Alternate Curtus B Kingsbury, Taunton, 63
Prospect Street)

BRISTOL SOUTH Edmond F Cody, New Bedford, 105 South
6th Street (Alternate Richard B Butler, Fall River,
278 North Main Street)

ESSEX NORTH Charles F Warren, Amesbury, 155 Main
Street (Alternate Percy J Look, Andover, 115 Main
Street)

ESSEX SOUTH Peer P Johnson, Beverly, 1 Monument Square
(Alternate De Witt S Clark Salem, 2 Oliver Street)

FRANKLIN John E Moran, Greenfield, 31 Federal Street
(Alternate Arthur W Hayes, Greenfield, 78 Federal
Street)

HAMPDEN Allen G Rice, Springfield, 146 Chestnut Street
(Alternate Harry F Byrnes, Springfield, 6 Chestnut
Street)

HAMPSHIRE Henry A Tadgell, Belchertown, Belchertown
State School (Alternate Lawrence N Durgin, Am-
herst, 66 Amity Street)

MIDDLESEX EAST Ralph R Stratton, Melrose (76) 538
Lynn Fells Parkway (Alternate Edward M Halligan,
Reading, 37 Salem Street)

MIDDLESEX NORTH Adam E Shaw, Lowell, 386 Andover
Street. (Alternate Walter L Twarog, Lowell, 117
Durant Street)

MIDDLESEX SOUTH Harold G Giddings, Newton Centre Office, Boston, 270 Commonwealth Avenue (Alternate Joseph C Merriam, Framingham, 198 Union Avenue)
 NORFOLK Albert Ehrenfried, Brookline Office, Boston (15), 520 Commonwealth Avenue (Alternate Carlton E Allard, Dorchester, 428 Columbia Road)
 NORFOLK SOUTH Daniel B Reardon, Quincy (69), 1186 Hancock Street (Alternate Frederick Hinchliffe, Cohasset, 117 South Main Street)
 PLYMOUTH Bradford H Peirce, South Hanson, Plymouth County Hospital (Alternate Alfred L Duncombe, Brockton, 38 Winthrop Street)
 SUFFOLK Albert A Hornor, Boston (15), 319 Longwood Avenue (Alternate Conrad Wesselhoeft, Boston, 315 Marlborough Street)
 WORCESTER Ralph S Perkins, Worcester, 10 Hackfeld Road (Alternate Franklyn P Bousquet, Worcester [8], 390 Main Street [interim appointment])
 WORCESTER NORTH John J Curley, Leominster, 89 West Street (Alternate James V McHugh, Leominster, 55 West Street)

STANDING COMMITTEES FOR 1946-1947

ELECTED BY THE COUNCIL, MAY 21, 1946

Date of Appointment

ARRANGEMENTS — Established 1849

Sidney C Wiggin, Suffolk June 24, 1942 (appointed chairman May 21, 1946)
 G Guy Bailey, Jr.,* November 13, 1942
 Middlesex South

John F Conlin, Suffolk May 21, 1946
 Harold G Giddings, May 22, 1944
 Middlesex South

Robert L Goodale, Suffolk May 22, 1944

ETHICS AND DISCIPLINE — Established 1871

Ralph R Stratton, June 9, 1936 (appointed chairman May 21, 1941)
 Middlesex East

William J Brickley, Suffolk February 3, 1937
 Archibald R Gardner, May 21, 1941
 Middlesex North

Fred R Jouett, May 21, 1940
 Middlesex South

Allen G Rice, Hampden June 1, 1938

FINANCE — Established 1938

Robert W Buck, May 21, 1946 (chairman)
 Middlesex South

Francis C Hall, Suffolk July 8, 1943

Fabyan Packard, May 21, 1946
 Middlesex South

Bancroft C Wheeler, May 21, 1946
 Worcester

Charles F Wilinsky, Suffolk June 2, 1938

INDUSTRIAL HEALTH — Established 1942

Daniel L Lynch, Norfolk May 25, 1942 (appointed chairman May 21, 1946)

Joseph C Aub, Suffolk May 25, 1942

Louis R Daniels, May 22, 1944
 Middlesex South

John G Downing, May 22, 1944
 Middlesex South

Patrick E Gear, Hampden May 23, 1945

Harold R Kurth, May 23, 1945
 Essex North

Thomas L Shipman, May 25, 1942
 Essex South

ADVISORY COMMITTEE TO COMMITTEE ON INDUSTRIAL HEALTH — Established 1942

Philip Drinker
 Harriet L Hardy
 Emma S Tousant

MEDICAL DEFENSE — Established 1927

Arthur W Allen, Suffolk June 7, 1927 (appointed chairman June 7, 1939)

Edwin D Gardner, June 7, 1927
 Bristol South

Charles J Kickham, Norfolk May 21, 1946

William R Morrison, Suffolk June 9, 1936

Horatio Rogers, Suffolk June 7, 1939

MEDICAL EDUCATION — Established 1881

Robert T Monroe, Norfolk May 21, 1941 (appointed chairman February 4, 1942)

James M Faulkner, Norfolk May 21, 1946

George D Henderson, June 1, 1938
 Hampden

Isaac R Jankelson, Norfolk May 25, 1942

Chester S Keefer, Suffolk February 4, 1942

MEMBERSHIP — Established 1897

Peirce H Leavitt, Plymouth June 1, 1938 (appointed chairman [interim appointment] September 3, 1946)

William A R Chapin, May 23, 1945
 Hampden

Lewis S Pilcher, July 26, 1946
 Middlesex South

(interim appointment)

Guy L Richardson, May 21, 1946
 Essex North

Samuel N Vose, Suffolk March 15, 1944

H Quimby Gallupe (Middlesex South), Albert E Parkhurst (Essex South), William F Ryan (Middlesex North) — representing the Supervising Censors

PUBLICATIONS — Established 1825

Richard M Smith, Suffolk June 6, 1933 (appointed chairman May 21, 1941)

Oliver Cope, Middlesex South May 21, 1941

John Fallon, Worcester November 14, 1944

James P O'Hare, Suffolk June 9, 1936

Conrad Wesselhoeft, Suffolk June 2, 1937

PUBLIC HEALTH — Established 1912

Roy J Ward, Worcester May 22, 1944 (chairman)

Elmer S Bagnall, Essex North May 23, 1945

John J Poustas, May 21, 1946
 Middlesex South

George L Steele, Hampden May 23, 1945

Conrad Wesselhoeft, Suffolk July 27, 1944

SOCIETY HEADQUARTERS — Established 1942

Frank R Ober, Suffolk May 22, 1944 (appointed chairman November 1, 1944)

Albert A Hornor, Suffolk November 6, 1944

Walter G Phippen, May 21, 1946
 Essex South

Daniel B Reardon, May 22, 1944
 Norfolk South

Michael A Tighe, May 24, 1943
 Middlesex North

SPECIAL COMMITTEES FOR 1946-1947

ELECTED BY THE COUNCIL, MAY 21, 1946

COMMITTEE ON CANCER — Established 1917

George A Moore (Plymouth), chairman, Thomas J Anglem, Suffolk, Ernest M Daland, Suffolk, Allen G Rice, Hampden, and Channing C Simmons, Suffolk.

COMMITTEE ON COUNCIL RULES — Established 1944

Charles E Morgan (Middlesex South), chairman, Elmer S Bagnall, Essex North, Frank R Ober, Suffolk, George L Schadt, Hampden, and Michael A Tighe, Middlesex North

COMMITTEE TO CONSIDER EXPERT TESTIMONY — Established 1936

Frank R Ober (Suffolk), chairman, Carl Bearse, Norfolk, William J Brickley, Suffolk, David Cheever, Suffolk, and Francis P McCarthy, Norfolk

COMMITTEE ON MATERNAL WELFARE — Established 1941

Raymond S Titus (Norfolk), chairman, James M Baty, Middlesex South, Ralph E Cole, Middlesex North, Arthur F G Edgelow, Hampden, Florence L McKay, Suffolk, Joseph C Merriam, Middlesex South, and Louis E Phaneuf, Suffolk

*Italics indicate that the physician is not a member of the Council

COMMITTEE TO MAKE A SURVEY OF MALPRACTICE INSURANCE IN MASSACHUSETTS — Established 1946

Carl Bearse (Norfolk), *chairman*, William J Brickley, Suffolk, Edwin D Gardner, Bristol South, Daniel B Reardon, Norfolk South, and Guy L Richardson, Essex North

COMMITTEE TO ASSIST THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS OF THE AMERICAN MEDICAL ASSOCIATION IN THE PROVISIONAL APPROVAL OF CERTAIN MASSACHUSETTS HOSPITALS — Established 1946

Robert T Monroe (Norfolk), *chairman*, H Quimby, Gallupe, Middlesex South, Walter G Phippen, Essex South, Michael A Tighe, Middlesex North, and Charles F Wilmsky, Suffolk

MEDICAL ADVISORY COMMITTEE TO REGIONAL OPA — Established 1945

Joseph Garland (Suffolk), *chairman*, F Gorham Brigham, Norfolk, Clifford L Derick, Middlesex South, Loring Grimes, Essex South, and Franklin W White, Suffolk

COMMITTEE ON PHYSICAL MEDICINE — Established 1945

Arthur L Watkins (Middlesex South), *chairman*, Ralph M Chambers, Bristol North, Franklin P Lozry, Middlesex South, Robert B Osgood, Suffolk, and Henry A Taddell, Hampshire

COMMITTEE ON POSTWAR LOAN FUND — Established 1945

George L Schadt (Hampden), *chairman*, Eliot Huhhard, Jr, Middlesex South, Charles C Lund, Suffolk, Albert E Parkhurst, Essex South, and Michael A Tighe, Middlesex North

COMMITTEE ON POSTWAR PLANNING — Established 1944

Howard F Root (Suffolk), *chairman*, Elmer S Bagnall, Essex North, George Ballantyne, Worcester, Vlado A. Gettung, Middlesex South, Charles J Kickham, Norfolk, Kenneth L MacLachlan, Middlesex East, Leland S McKittrick, Suffolk, Robert N Nye, Suffolk, W Richard Ohler, Norfolk, Leroy E Parkins, Suffolk, and Walter G Phippen, Essex South

Subcommittees of the Committee on Postwar Planning

Co-ordinating on Education — Established 1944

Charles F Branch, Suffolk, Nathaniel W Faxon, Suffolk, and W Richard Ohler, Norfolk

HOSPITALS — Established 1944

Charles F Wilmsky (Suffolk), *chairman*, Arthur W Allen, Suffolk, Nathaniel W Faxon, Suffolk, Harold Jeghers, Norfolk, James W Manary, Suffolk, and Clifton T Perkins, Middlesex East

MEDICAL ECONOMICS — Established 1944

Leland S McKittrick (Suffolk), *chairman*, Elmer S Bagnall, Essex North, Allan M. Butler, Suffolk, Vlado A. Gettung, Middlesex South, and Merrill C Sosman, Suffolk

MEDICAL SCHOOLS — Established 1944

Charles F Branch (Suffolk), *chairman*, C Sidney Burzell, Norfolk, and Walter G Phippen, Essex South

ORGANIZATION — Established 1944

Walter G Phippen (Essex South), *chairman*, George Ballantyne, Worcester, Frederick S Hopkins, Hampden, Chester M Jones, Suffolk, Frank R. Ober, Suffolk, Joseph W O'Connor, Worcester, Francis J Steele, Worcester, and Michael A Tighe, Middlesex North

POSTGRADUATE MEDICAL EDUCATION — Established 1944

W Richard Ohler (Norfolk), *chairman*, Vlado A. Gettung, Middlesex South, G Philip Grabfield, Suffolk, Lewis M Horvath, Suffolk, Charles J Kickham, Norfolk, Eugene M Landis, Middlesex South, Charles G Mixer, Suffolk, Robert N Nye, Suffolk, Joseph W O'Connor, Worcester, Samuel H Proger, Norfolk, and Harry C Solomon, Suffolk

COMMITTEE ON VETERANS' AFFAIRS — Established 1946

G Philip Grabfield (Suffolk), *chairman*, Victor G Balboni, Suffolk, George P Denny, Suffolk, Alexander Marble, Suffolk, and George F Wilkins, Middlesex South

In addition the following are representatives from the various district medical societies

Charles Bradford,* Suffolk
Stephen Brown,* Hampshire
William M Carr,* Plymouth
Leo R Desmond,* Norfolk
Spencer C Flo,* Franklin
Merrill F Gardner,* Bristol South
Willis M Gowen,* Middlesex East
Leonard W Hill,* Bristol North
Sheldon L Hart,* Barnstable
Thomas Hunter,* Worcester
John C McGirr,* Middlesex South
Franklin K Paddock,* Berkshire
Ensis K F Ronka,* Norfolk South
Louis B Simard,* Essex North
Thomas J G Tighe,* Middlesex North

AUDITING COMMITTEE

Howard B Jackson (Norfolk), *chairman*, and Frank T Downey, Middlesex South (interim appointment)

COMMITTEE ON POSTGRADUATE ASSEMBLY — Established 1946

Leroy E Parkins (Suffolk), *chairman*, Harold G Giddings, Middlesex South, Frederick S Hopkins, Hampden, Charles J Kickham, Norfolk, and Robert N Nye, Suffolk

COMMITTEE ON REHABILITATION — Established 1941

Joseph H Shortell (Suffolk), *chairman*, Benjamin F Andrews, Worcester, Ralph M Chambers, Bristol North, William M Collins, Middlesex North, James J Regan, Suffolk, and Arthur L Watkins, Middlesex South

COMMITTEE TO MAKE RECOMMENDATIONS AS TO FUTURE DIRECTORS OF THE BLUE SHIELD — Established 1945

Leland S McKittrick (Suffolk), *chairman* (term expires May 1949), Harold G Giddings, Middlesex South (term expires May, 1951), Elliott P Joslin, Suffolk (term expires May, 1947), Peirce H Leavitt, Plymouth (term expires May, 1950), and George Gilbert Smith, Suffolk (term expires May, 1948)

COMMITTEE TO MEET WITH THE MASSACHUSETTS HOSPITAL ASSOCIATION — Established 1940

Walter G Phippen (Essex South), *chairman*, Edward A Adams, Worcester North, Nicholas S Scarcello, Worcester (interim appointment), Edwin D Gardner, Bristol South, Frederic Hagler, Hampden, and Albert E Parkhurst, Essex South

COMMITTEE TO CONFER WITH THE MASSACHUSETTS FARM BUREAU FEDERATION — Established 1945

Joseph C Merriam (Middlesex South), *chairman*, John E Moran, Franklin, and Elmer E Thomas, Hampshire (interim appointment)

COMMITTEE TO SURVEY SALARIES — Established 1946

Charles J Kickham (Norfolk), *chairman* (interim appointment), Robert W Buck, Middlesex South (interim appointment), and Robert N Nye, Suffolk (interim appointment)

COMMITTEE TO STUDY INCREASE IN ASSESSMENT OF DUES — Established 1946

Frank R Ober (Suffolk), *chairman* (interim appointment), N Newall Copeland, Berkshire (interim appointment), Edwin D Gardner, Bristol South (interim appointment), Kenneth L MacLachlan, Middlesex East (interim appointment), and John W McKeon, Worcester (interim appointment)

*Interim appointment.

COMMITTEE TO STUDY INCOME LEVEL FOR BLUE SHIELD — Established 1946

Charles F. Wihnsky (Suffolk), *chairman* (interim appointment), *Norman H. Bruce*, Middlesex South (interim appointment), Raoul L. Drapeau, Middlesex North (interim appointment), Henry L. Kirkendall, Worcester (interim appointment), and John W. Spellman, Norfolk (interim appointment)

COMMITTEE OF SEVEN — Established 1946

Elmer S. Bagnall, Essex North, David Cheever, Suffolk, Roger I. Lee, Suffolk, Charles E. Mongan, Middlesex South, Frank R. Ober, Suffolk, Walter G. Phippen, Essex South, and George L. Schadt, Hampden

COMMITTEE TO MEET WITH GENERAL HAWLEY WITH VIEW OF FORMULATING PROGRAM IN MASSACHUSETTS FOR MEDICAL CARE OF VETERANS AND THEIR DE- PENDENTS — Established 1945

Humphrey L. McCarthy (Norfolk), *chairman*, James K. Bragger, Norfolk (interim appointment), and Michael A. Tighe, Middlesex North

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

George D. Henderson (Hampden), *chairman*, Elmer S. Bagnall, Essex North, James W. Bunce, Berkshire, Merrill E. Champion, Suffolk, and Robert B. Orgood, Suffolk

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR THE YEAR 1946

William E. Browne, Suffolk

REPRESENTATIVE ON THE LEGISLATIVE COMMITTEE OF THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

William E. Browne, Suffolk

REPRESENTATIVE ON A PROFESSIONAL ADVISORY COMMITTEE ORGANIZED BY THE DIVISION OF VOCATIONAL RE- HABILITATION OF STATE DEPARTMENT OF EDUCA- TION FOR PURPOSE OF ESTABLISHING A PROGRAM ON PHYSICAL RESTORATION

Joseph H. Shortell, Suffolk

REPRESENTATIVES TO THE COUNCIL OF THE NEW ENGLAND STATE MEDICAL SOCIETIES

Allen G. Rice, Hampden, Michael A. Tighe, Middlesex North, and Norman A. Welch, Norfolk (interim appointment)

REPRESENTATIVE FOR SURVEY BY ACADEMY OF PEDIATRICS Gerald N. Hoefel, Middlesex South (interim appoint- ment)

TWENTY-FIVE VOTING MEMBERS IN MASSACHUSETTS HOSPITAL SERVICE, INC

Benjamin H. Alton, Worcester, Gerardo M. Balboni, Suffolk, Laurence D. Chapin, Hampden, Lucien R. Chaput, Essex North, Hilbert F. Day, Middlesex South, George K. Fenn, Essex South, Joseph E. Flynn, Middlesex South, Archibald R. Gardner, Middlesex North, Harold G. Giddings, Middlesex South, Henry W. Godfrey, Middlesex South, Albert A. Hornor, Suffolk, John H. Lambert, Middlesex North, Alexander A. Levi, Middlesex South, Raymond A. McCarthy, Middlesex South, Joseph C. Merriam, Middlesex South, Donald Munro, Suffolk, Albert E. Parkhurst, Essex South, Lewis S. Pilcher, Middlesex South, Helen S. Pittman, Suffolk, Allen G. Rice, Hampden, Arthur T. Ronan, Norfolk, George L. Steele, Hampden, Ralph R. Stratton, Middlesex East, John E. Talbot, Worcester, and Edward L. Young, Norfolk

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION FOR 1946-1947

DELEGATES

ALTERNATES

June 1, 1945, to June 1, 1947

Charles J. Kickham,
Norfolk
Leland S. McKuttrick,
Suffolk

John Fallon,
Worcester
Patrick J. Sullivan,
Berkshire

June 1, 1946, to June 1, 1948

David D. Scannell,
Norfolk
Dwight O'Hara,
Middlesex South
Charles E. Mongan,
Middlesex South
Walter G. Phippen,
Essex South
Elmer S. Bagnall,
Essex North
William J. Pelletier,
Franklin
Patrick E. Gear,
Hampden
John I. B. Vail,
Barnstable

COUNCILORS FOR 1946-1947

(ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR
ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1946)

BARNSTABLE

H. F. Rowley, Harwich Port, V. P.
P. M. Butterfield, Harwich, E. C., M. N. C.
P. P. Henson, Hyannis, 149 Main St., A. E. C., A. M. N. C., P. R. C.
C. H. Keene, Chatham, Seaview St.
O. S. Simpson, Centerville, Main St., Sec.

BERKSHIRE

N. N. Copeland, Pittsfield, 131 North St., V. P.
D. N. Beers, Pittsfield, 74 North St., Sec.
I. S. F. Dodd, Pittsfield, 34 Fenn St., Vice-President, E. C.
John Hughes, Pittsfield, 74 North St., A. M. N. C., Leg. C.
C. F. Kernan, Pittsfield, 184 North St., A. E. C.
Solomon Schwager, Pittsfield, 246 North St.
Helen M. Scoville, Pittsfield, House of Mercy Hospital
P. J. Sullivan, Dalton, 471 Main St., M. N. C., P. R. C.
E. R. Wyman, Great Barrington, 259 Main St.

BRISTOL NORTH

W. M. Stobbs, Attleboro, 63 Bank St., V. P.
W. H. Allen, Mansfield, 70 North Main St.
M. E. Johnson, Attleboro, 33 Bank St., P. R. C.
C. B. Kingsbury, Taunton, 63 Prospect St., A. E. C., A. M. N. C., Leg. C.
W. J. Morse, Attleboro, 34 Sanford St., Sec.
J. L. Murphy, Taunton, 23 Cedar St., E. C., M. N. C.

BRISTOL SOUTH

S. P. Wilde, New Bedford, 73 Borden St., V. P.
R. B. Butler, Fall River, 278 North Main St., E. C., A. M. N. C.
E. F. Cody, New Bedford, 105 South Sixth St., M. N. C.
J. C. Corrigan, Fall River, 422 North Main St.
J. E. Fell, Fall River, 181 Purchase St., Sec.
J. A. Fournier, Fall River, 11 Choate St.
E. D. Gardner, Marion, Box 175.
R. H. Goodwin, New Bedford, 15 South 6th St.
William Mason, Fall River, 151 Rock St.
D. R. Mills, Edgartown, Pease Point Way.
H. E. Perry, New Bedford, 159 Cottage St., P. R. C.
C. C. Tripp, New Bedford, 416 County St., A. E. C., Leg. C.
Henry Wardle, Fall River, 173 Purchase St.

ESSEX NORTH

G. L. Richardson, Haverhill, 94 Emerson St., V. P.
E. S. Bagnall, Groveland, 281 Main St., Ex-Pres.
R. V. Baketel, Methuen, 7 Hampshire St.
R. E. Blas, Amesbury, 165 Main St.
G. J. Connor, Haverhill, 81 Merrimack St., A. E. C.
Elizabeth Councilman, Newburyport, 83 High St.
N. F. DeCesare, Lawrence, 57 Jackson St., Leg. C.
H. A. Fenton, Lawrence, 36 Winthrop Ave.
H. R. Kurth, Lawrence, 57 Jackson St., Sec., P. R. C.
P. J. Look, Andover, 115 Main St., A. M. N. C.
R. J. Neil, Methuen, 255 Broadway.
R. C. Norris, Methuen, 247 Broadway, E. C.
F. W. Snow, Newburyport, 24 Essex St.
C. F. Warren, Amesbury, 1 School St., M. N. C.

ESSEX SOUTH

C. A. Worthen, Lynn, 19 Park St., V. P.
K. J. Chadwell, Swampscott, 26 Lexington Circle.
D. S. Clark, Salem, 2 Oliver St., A. M. N. C.
R. E. Foss, Peabody, 125 Main St.
Loring Grimes, Swampscott, 84 Humphrey St., P. R. C.
C. A. Hernck, Manchester, 21 Union St.
W. R. Irving, Gloucester, 35 Middle St.
P. P. Johnson, Beverly, 1 Monument Sq., M. N. C.
H. M. Lowd, Swampscott, 90 Burial St.

B B Mansfield, Ipswich, 4 Green St
A E Parkhurst, Beverly, 1 Monument Sq
O S Pettingill, Middleton, Essex Sanatorium
W G Phippen, Salem, 31 Chestnut St, Ex-Pres, E C
E D Reynolds, Danvers, 48 High St
J R Shaughnessey, Salem, 24½ Winter St
H D Stebbins, Salem, 342 Essex St, Sec
P E Tivnan, Salem, 70 Washington St
C F Twomey, East Lynn, 80 Ocean St

FRANKLIN

J B Temple, Shelburne Falls, 11 Main St, V P
H L Craft, Ashfield, Sec.
A W Hayes, Greenfield, 78 Federal St, A M N C,
Leg C
F A Millett, Greenfield, 40 High St, A E C, P R C
J E Moran, Greenfield, 31 Federal St, E C, M N C

HAMPTDEN

Adolph Franz, Jr, Holyoke, 1158 Northampton St,
V P
F H Allen, Holyoke, 16 Fairfield St
E P Bagg, Holyoke, 207 Elm St, President-Elect
J M Birnie, Springfield, 146 Chestnut St, Ex-Pres
H F Byrnes, Springfield, 6 Chestnut St, A M N C
W A R. Chapin, Springfield, 121 Chestnut St, E C
J L Chereskin, Springfield, 333 Bridge St
A J Douglas, Westfield, 30 Court St, A E C
E C Dubois, Springfield, 174 Buckingham St
P E Gear, Holyoke, 188 Chestnut St, P R C
Frederic Hagler, Springfield, 20 Maple St
G D Henderson, Holyoke, 176 Chestnut St
F S Hopkins, Springfield, 146 Chestnut St
Charles Jurst, Springfield, 70 Chestnut St
M W Pearson, Ware, 19 Pleasant St
A G Rice, Springfield, 146 Chestnut St, M N C
A H Riordan, Indian Orchard, 147 Oak St, Leg C
G L Schadt, Springfield, 44 Chestnut St, Ex-Pres
J A Seaman, Longmeadow, Office Springfield, 20
Maple St
G C Steele, West Springfield, 39 Upper Church St, Sec.
G L Steele, Springfield, 20 Maple St
W W Teahan, Holyoke, 217 Essex St.

HAMPSHIRE

J J Curran, Northampton, 16 Centre St, V P
L N Dargin, Amherst, 66 Amity St., A E C, A M
N C, Leg C
J R Hobbs, Williamsburg, Main St., P R C
L B Pond, Easthampton, 115 Main St
Mary P Snook, Worthington, Sec.
H A Tadgell, Belchertown, Belchertown State School,
E C, M N C

MIDDLESEX EAST

W H Flanders, Melrose 76, 481 Lebanon St, V P
J L Anderson, Reading, 53 Woburn St, A E C
Robert Dutton, Wakefield, 33 Avon St
E. M. Halligan, Reading, 37 Salem St, A M N C
R W Layton, Melrose 76, 8 Porter St, Sec.
K. L. MacLachlan, Melrose 76, 1 Bellevue Avenue, E C
M J Quinn, Winchester, 44 Church St, P R C
W F Regan, Winchester, 101 High St
R. R. Stratton, Melrose 76, 538 Lynn Fells Parkway,
M N C, C
J M Wilcox, Woburn, 6 Bennett St., Leg C

MIDDLESEX NORTH

W F Ryan, Lowell, 219 Central St., V P, E C
R L Drapeau, Dracut, 1346 Bridge St
D J Ellison, Lowell, 8 Merrimack St, P R C
A R Gardner, Lowell, 16 Shattuck St, Leg C
S G Hajjar, North Billerica, 2 Talbot Ave
B D Leabeey, Lowell, 9 Central St, Sec.
A E Shaw, Lowell, 386 Andover St, M N C
M A Tighe, Lowell, 9 Central St, Sec
W L Twarog, Lowell, 117 Durant St., A E C, A M
N C

MIDDLESEX SOUTH

J F Casey, Allston, Office Boston 15, 475 Common-
wealth Ave., V P

E W Barron, Malden 48, Office Boston, 20 Ash St
Harris Bass, Everett 49, 351 Broadway
J M Baty, Belmont, Office Brookline 46, 1101 Bea-
con St
I D Bennett, West Somerville 44, 72 College Ave
E. H. Bigelow, Framingham Centre, 65 Edgell Rd, Ex-
Pres
W O Blanchard, Newton 58, 465 Centre St
G F H Bowers, Newton Highlands 61, 156 Wood-
ward St
Alice M Broadhurst, Watertown 72, 259 Mt Auburn St
Madeline R Brown, Cambridge, Office Boston 16,
264 Beacon St
R N Brown, Malden 48, 621 Main St
R W Buck, Waban, Office Boston 15, 5 Bay State Rd, C
E J Butler, Cambridge, 25 Garden St
C W Clark, Newtonville 60, 363 Walnut St
J A Daley, Natick, 36 Pond St
H F Day, Cambridge, 34 Kirkland St
C L Derick, Newton Highlands, Office Boston 15,
412 Beacon St
J G Downing, Newton, Office Boston 15, 520 Common-
wealth Ave
C W Finnerty, West Somerville 44, 440 Broadway
H Q Gallupe, Waltham 54, 751 Main St
F W Gay, Malden 48, 20 Park St
V A Getting, Belmont, Office Boston 8, 546 State House
H G Giddings, Newton Centre, Office Boston 16,
270 Commonwealth Ave, E C, M N C
H W Godfrey, Auburndale 66, 14 Hancock St
J L Golden, Medford 55, 86 Forest St
A D Guthrie, Medford 55, 408 Salem St
Eliot Hubbard, Jr, Cambridge, 29 Highland St, Treas-
urer
A M Jackson, Everett 49, 512 Broadway, A E C
F R Jouett, Cambridge, 1 Craigie St
E E Kattwinkel, West Newton 65, 65 Sterling St.
A A Levi, Newton, Office Boston 15, 481 Beacon St.,
Sec.
A N Makechnie, Cambridge, 14 Upland St
R A McCarty, Waltham 54, 465 Lexington St
P H Means, Cambridge, 1 Waterhouse St
J C Merrim, Framingham, 198 Union Ave, A M N C
Dudley Merrill, Cambridge, 51 Brattle St
C E Mongan, Somerville 43, 24 Central St., Ex-Pres
G M Morrison, Waban, Office Boston 15, 520 Common-
wealth Ave., P R C
J P Nelligan, Cambridge, 2336 Massachusetts Ave.
E J O'Brien, Jr, Newton, Office Boston 16, 270 Com-
monwealth Ave
Dwight O'Hara, Waltham, Office Boston 15, 416 Hunt-
ington Ave, President.
Fabyan Packard, Belmont, Office Boston, Soldiers'
Field
L G Paul, Newton Centre, Office Boston 16, 270
Commonwealth Ave.
L S Pilcher, Newton Centre 59, 45 Parker St
Randolph Piper Concord, 14 Sndbury Rd
T E Reilly, Marlboro, 6 Newton St
S H Remick, Waltham 54, 735 Trapelo Rd
Max Ritvo, Newton, Office Boston 15, 416 Marlborough St.
E H Robbins, Somerville 43, 334 Broadway
M J Schlesinger, Newton, Office Boston 15,
330 Brookline Ave.
E W Small, Belmont 78, 68 Leonard St
H P Stevens, Cambridge, 1 Craigie St
K J Tillotson, Waverley 79, McLean Hospital, Leg C
A B Toppin, Watertown 72, 289 Mt Auburn St
J E Vance, Natick, Office Boston 15, 29 Bay State Rd
Fresenius Van Nüys, Weston 93, 338 Boston Post Rd
C F Walcott, Cambridge, 81 Sparks St
A L Watkins, Arlington, Office Boston 14, Massachu-
setts General Hospital
B M Wein, Newton, Office Boston 15, 471 Common-
wealth Ave.
B S Wood, Weston, Office Waltham 54, 751 Main St.
Alfred Worcester, Waltham 54, 314 Bacon St, Ex-Pres
Hovhaunes Zovickian, Watertown 72, 528 Mt Auburn St.

NORFOLK

J H Cauley, Dorchester, 8 Carruth St, V P
A A Abrams, Brookline 46, 153 Dean Rd

COMMITTEE TO STUDY INCOME LEVEL FOR BLUE SHIELD — Established 1946

Charles F Wilinsky (Suffolk), *chairman* (interim appointment), *Norman H Bruce*, Middlesex South (interim appointment), Raoul L Drapeau, Middlesex North (interim appointment), Henry L Kirkendall, Worcester (interim appointment), and John W Spellman, Norfolk (interim appointment)

COMMITTEE OF SEVEN — Established 1946

Elmer S Bagnall, Essex North, David Cheever, Suffolk, Roger I Lee, Suffolk, Charles E Mongan, Middlesex South, Frank R Ober, Suffolk, Walter G Phippen, Essex South, and George L Schadt, Hampden

COMMITTEE TO MEET WITH GENERAL HAWLEY WITH VIEW OF FORMULATING PROGRAM IN MASSACHUSETTS FOR MEDICAL CARE OF VETERANS AND THEIR DEPENDENTS — Established 1945

Humphrey L McCarthy (Norfolk), *chairman*, James K Bragger, Norfolk (interim appointment), and Michael A Tighe, Middlesex North

REPRESENTATIVES TO THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

George D Henderson (Hampden), *chairman*, Elmer S Bagnall, Essex North, James W Bunce, Berkshire, Merrill E Champion, Suffolk, and Robert B Orgood, Suffolk

REPRESENTATIVE TO THE HOSPITAL COUNCIL OF BOSTON FOR THE YEAR 1946

William E Browne, Suffolk

REPRESENTATIVE ON THE LEGISLATIVE COMMITTEE OF THE MASSACHUSETTS CENTRAL HEALTH COUNCIL

William E Browne, Suffolk

REPRESENTATIVE ON A PROFESSIONAL ADVISORY COMMITTEE ORGANIZED BY THE DIVISION OF VOCATIONAL REHABILITATION OF STATE DEPARTMENT OF EDUCATION FOR PURPOSE OF ESTABLISHING A PROGRAM ON PHYSICAL RESTORATION

Joseph H Shortell, Suffolk

REPRESENTATIVES TO THE COUNCIL OF THE NEW ENGLAND STATE MEDICAL SOCIETIES

Allen G Rice, Hampden, Michael A Tighe, Middlesex North, and Norman A Welch, Norfolk (interim appointment)

REPRESENTATIVE FOR SURVEY BY ACADEMY OF PERIATRICS

Gerald N Hoeffel, Middlesex South (interim appointment)

TWENTY-FIVE VOTING MEMBERS IN MASSACHUSETTS HOSPITAL SERVICE, INC

Benjamin H Alton, Worcester, Gerardo M Balboni, Suffolk, Laurence D Chapin, Hampden, Lucien R Chapui, Essex North, Hilbert F Day, Middlesex South, George K Fenn, Essex South, Joseph E Flynn, Middlesex South, Archibald R Gardner, Middlesex North, Harold G Giddings, Middlesex South, Henry W Godfrey, Middlesex South, Albert A Hornor, Suffolk, John H Lambert, Middlesex North, Alexander A Levi, Middlesex South, Raymond A McCarthy, Middlesex South, Joseph C Merriam, Middlesex South, Donald Munro, Suffolk, Albert E Parkhurst, Essex South, Lewis S Pilcher, Middlesex South, Helen S Pittman, Suffolk, Allen G Rice, Hampden, Arthur T Ronan, Norfolk, George L Steele, Hampden, Ralph R Stratton, Middlesex East, John E Talbot, Worcester, and Edward L Young, Norfolk

DELEGATES AND ALTERNATES TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION FOR 1946-1947

DELEGATES ALTERNATES

June 1, 1945, to June 1, 1947

Charles J Kickham, John Fallon, Norfolk, Worcester
Leland S McKittick, Patrick J Sullivan, Suffolk, Berkshire

June 1, 1946, to June 1, 1948

David D Scannell, Elmer S Bagnall, Norfolk, Essex North
Dwight O'Hara, William J Pelletier, Middlesex South, Franklin
Charles E Mongan, Patrick E Gear, Middlesex South, Hampden
Walter G Phippen, John I B Fain, Essex South, Barnstable

COUNCILORS FOR 1946-1947

(ELECTED BY THE DISTRICT MEDICAL SOCIETIES AT THEIR ANNUAL MEETINGS, APRIL 15 TO MAY 15, 1946)

BARNSTABLE

H F Rowley, Harwich Port, V P
P M Butterfield, Harwich, E C, M N C
P P Henson, Hyannis, 149 Main St, A E C, A M N C, P R C
C H Keene, Chatham, Seaview St
O S Simpson, Centerville, Main St, Sec

BERKSHIRE

N N Copeland, Pittsfield, 131 North St, V P
D N Beers, Pittsfield, 74 North St, Sec
I S F Dodd, Pittsfield, 34 Fenn St, Vice-President, E C
John Hughes, Pittsfield, 74 North St, A M N C, Leg C
C F Kernan, Pittsfield, 184 North St, A E C
Solomon Schwager, Pittsfield, 246 North St
Helen M Scoville, Pittsfield, House of Mercy Hospital
P J Sullivan, Dalton, 471 Main St, M N C, P R C
E R Wyman, Great Barrington, 259 Main St

BRISTOL NORTH

W M Stobbs, Attleboro, 63 Bank St, V P
W H Allen, Mansfield, 70 North Main St
M E Johnson, Attleboro, 33 Bank St, P R C
C B Kingsbury, Taunton, 63 Prospect St, A E C, A M N C, Leg C
W J Morse, Attleboro, 34 Sanford St, Sec
J L Murphy, Taunton, 23 Cedar St, E C, M N C

BRISTOL SOUTH

S P Wilde, New Bedford, 73 Borden St, V P
R B Butler, Fall River, 278 North Main St, E C, A M N C
E F Cody, New Bedford, 105 South Sixth St, M N C
J C Corrigan, Fall River, 422 North Main St
J E Fell, Fall River, 181 Purchase St, Sec
J A Fournier, Fall River, 11 Choate St
E D Gardner, Manon, Box 175
R H Goodwin, New Bedford, 15 South 6th St
William Mason, Fall River, 151 Rock St
D R Mills, Edgartown, Pease Point Way
H E Perry, New Bedford, 159 Cottage St, P R C
C C Tripp, New Bedford, 416 County St, A E C, Leg C
Henry Wardle, Fall River, 173 Purchase St

ESSEX NORTH

G L Richardson, Haverhill, 94 Emerson St, V P
E S Bagnall, Groveland, 281 Main St, Ex-Prca
R V Baketel, Methuen, 7 Hampshire St
R E Bias, Amesbury, 165 Main St
G J Connor, Haverhill, 81 Merrimack St, A E C
Elizabeth Councilman, Newburyport, 83 High St
N F DeCesare, Lawrence, 57 Jackson St, Leg C
H A Fenton, Lawrence, 36 Winthrop Ave
H R Kurth, Lawrence, 57 Jackson St, Sec, P R C
P J Look, Andover, 115 Main St, A M N C
R J Neil, Methuen, 255 Broadway
R C Norris, Methuen, 247 Broadway, E C
F W Snow, Newburyport, 24 Essex St
C F Warren, Amesbury, 1 School St, M N C

ESSEX SOUTH

C A Worthen, Lynn, 19 Park St, V P
K J Chadwell, Swampscott, 26 Lexington Circle
D S Clark, Salem, 2 Oliver St, A M N C
R E Foss, Peabody, 125 Main St
Loring Grimes, Swampscott, 84 Humphrey St, P R C
C A Herrick, Manchester, 21 Union St
W R Irving, Gloucester, 35 Middle St
P P Johnson, Beverly, 1 Monument Sq, M N C
H M Lowd, Swampscott, 90 Burill St

Conrad Wesselhoeft, Boston, 315 Marlborough St.,
A M N C
C F Wilinsky, Boston 15, 330 Brookline Ave

WORCESTER

L M Felton, Worcester, 36 Pleasant St, V P
C R Abbott, Clinton, 60 Walnut St
A W Atwood, Worcester, 390 Main St
George Ballantyne, Worcester, 27 Elm St
F P Bousquet, Worcester (8), 390 Main St, A E C,
A M N C. (interim appointment)
W P Bowers, Clinton, 264 Chestnut St, Ex-Pres
J J Cohen, Worcester, 340 Main St
E J Crane, Holden, Armington Lane
G R Dunlop, Worcester, 27 Elm St, Leg C
W J Elliott, Worcester, 119 Belmont St
John Fallon, Worcester, 390 Main St
R H Goodale, Worcester, 36 Otsego Rd
Thomas Hunter, Shrewsbury, 545 Main St
H L Kirkendall, Worcester, 27 Elm St
J A Lundy, Oxford, 26 Main St
D K McClusky, Worcester, 7 Hawthorne St
J M Olson, Westboro, 54 West Main St
F A O'Toole, Clinton, 181 Chestnut St
R S Perkins, Worcester, 27 Elm St, M N C
E L Richmond, Worcester (8), 390 Main St (interim
appointment)
N S Scarcello, Worcester, 1 Shelden St, P R C
R F Sullivan, Worcester, 54 Hillcroft Ave
J J Tegelberg, Worcester, 390 Main St, Sec
G C Tully, Worcester, 1 Cedar St
R J Ward, Worcester, 9 Bellevue St, C
B C Wheeler, Worcester, 27 Elm St, E C

WORCESTER NORTH

R F Bachmann, Fitchburg, 910 Main St, V P
H C Arey, Gardner, 66 Parker St
D B Cheatham, Athol, 164 Exchange St
J J Curley, Leominster, 89 West St, A E C, M N C,
Leg C
C B Gay, Fitchburg, 62 Day St, E C
J V McHugh, Leominster, 55 West St, A M N C,
P R C
J G Simmons, Fitchburg, 30 Myrtle Ave, Sec

The initials E C following the name of a counselor indicate that he is a member of the Executive Committee and A E C that he is an alternate member of the Executive Committee. M N C that he is a member of the Committee on Nominations, and A M N C that he is an alternate member of the Committee on Nominations. Leg C that he is a member of the Committee on Legislation. P R C that he is a member of the Committee on Public Relations. V P that a member is a counselor by virtue of his office as president of a district society and so vice president of the general society. C by virtue of his office as chairman of a standing committee. Sec by virtue of his office as secretary of a district society and Ex Pres by virtue of being a past president

CENSORS FOR 1946-1947

BARNSTABLE

(Supervisor to be appointed)
E F Curry, Sagamore
J I B Vail, Hyannis
D H Hiebert, Provincetown
Frank Travers, Barnstable

BERKSHIRE

I S F Dodd, Pittsfield, supervisor
A C England, Pittsfield
W T Frawley, Pittsfield
C T Leslie, Pittsfield
J W Bunce, North Adams

BRISTOL NORTH

J L Murphy, Taunton, supervisor
H G Vaughan, Attleboro
A J Leddy, Taunton
L E Butler, Taunton
J H Brewster, Attleboro

BRISTOL SOUTH

Henry Wardle, Fall River, supervisor
E A McCarthy, Fall River
F M Howes, New Bedford
W F MacKnight, Fall River
C C Persons, New Bedford

ESSEX NORTH

R V Baketel, Methuen, supervisor
L C Peirce, Newburyport
C H Birdsall, Haverhill
Abraham Ash, Lawrence
F R Radcliffe, Haverhill

ESSEX SOUTH

A E Parkhurst, Beverly, supervisor
S N Gardner, Salem
W C Inman, Danvers
C F Twomey, Lynn
H N Baker, Rockport

FRANKLIN

J E Moran, Greenfield, supervisor
W J Pelletier, Turners Falls
J P Collieran, South Deerfield
H R Mahar, Orange
F W Dean, Northfield

HAMPDEN

Frederic Hagler, Springfield, supervisor
J M Gilchrist, Springfield
G D Henderson, Holyoke
John Pallo, Westfield
J L Smead, Springfield

HAMPSHIRE

L B Pond, Easthampton, supervisor
T F Corriden, Northampton
M E Cooney, Northampton
J E Hayes, Northampton
Stephen Brown, Northampton

MIDDLESEX EAST

M J Quinn, Winchester, supervisor
J H Fay, Melrose
S H Moses, Winchester
C R Baisley, Reading
T P Devlin, Stoneham

MIDDLESEX NORTH

W F Ryan, Lowell, supervisor
F R Brady, Lowell
R C Stewart, Lowell
H L Leland, Lowell
J D Sweeney, Lowell

MIDDLESEX SOUTH

H Q Gallupe, Waltham, supervisor
E H Robbins, Somerville
J E Dodd, Framingham
J F Williams, Everett
H J Crumb, Lexington

NORFOLK

Hyman Morrison, Roxbury, supervisor
C E Allard, Dorchester
H A Novack, Brookline
E E O'Neil, Chestnut Hill
Kathleyne S Snow, Jamaica Plain

NORFOLK SOUTH

F A Bartlett, Wollaston, supervisor (interim appointment)
R E Ross, South Braintree
W L Sargent, Quincy
Arthur Rapoport, Quincy
H S Reid, Cohasset

PLYMOUTH

E L Perry, Middleboro, supervisor
D W Pope, Brockton
R E Swenson, Plymouth
G A Buckley, Brockton
Jacob Brenner, North Easton

C E Allard, Dorchester, 428 Columbia Rd, A M N C
 B E Barton, West Roxbury 32, 10 Richwood St, Sec
 Carl Bearse, Boston 15, 483 Beacon St
 Arthur Berk, Brookline, Office Boston 16, 270 Commonwealth Ave
 D J Collins, Norwood, 100 Day St
 William Dameshek, Brookline, Office Boston 15, 113 Bay State Rd
 G L Doherty, West Roxbury, Office Boston 15, 466 Commonwealth Ave
 Albert Ehrenfried, Brookline, Office Boston 15, 520 Beacon St, M N C
 H M Emmons, Needham, Office Boston 15, 354 Commonwealth Ave
 Susannah Friedman, Roxbury, Office Boston 15, 485 Commonwealth Ave
 B A Godvin, Jamaica Plain, Office Boston 15, 483 Beacon St
 D L Halbersleben, Brookline 46, 42 Goodnough Rd
 J B Hall, Roxbury 19, 108 Dudley St
 H B Harris, East Milton, Office Dorchester, 487 Columbia Rd
 R J Heffernan, Jamaica Plain, Office Brookline 46, 1101 Beacon St
 P J Jakmauh, Milton, Office South Boston 27, 509 Broadway
 I R Jankelson, Jamaica Plain, Office Boston 15, 483 Beacon St
 C J Kickham, Brookline, Office Boston 15, 508 Commonwealth Ave, E C
 C J E Kickham, Jamaica Plain, Office Brookline 46, 1101 Beacon St
 D L Lionberger, Dedham, 709 East St
 D S Luce, Canton, 553 Washington St, P R C
 C M Lydon, Dorchester, 276 Bowdoin St
 D L Lynch, Roslindale, Office Boston, 245 State St, C
 F P McCarthy, Milton, Office Boston 15, 371 Commonwealth Ave
 H L McCarthy, West Roxbury, Office Boston 15, 479 Beacon St
 R T Monroe, Brookline, Office Boston 16, 270 Commonwealth Ave, C
 F J Moran, Dedham, 395 Washington St
 Hyman Morrison, Brookline, Office Boston 15, 483 Beacon St
 D J Mullane, Brookline 46, 1101 Beacon St
 J J O'Connell, Dorchester, 1061 Dorchester Ave
 W R Ohler, Jamaica Plain, Office Boston 15, 319 Longwood Ave
 G W Papen, Brookline, Office Boston, 31 Milk St
 H C Petterson, West Roxbury, Office Boston 15, 29 Bay State Rd
 Frederick Reis, Jamaica Plain, Office Boston 15, 416 Huntington Ave
 H A Rice, Canton, 742 Washington St
 S A Robins, Boston 15, 636 Beacon St
 D D Scannell, Jamaica Plain, Office Boston 15, 475 Commonwealth Ave
 J A Seth, Milton, Office Boston 15, 47 Bay State Rd
 J A Sieracki, Norwood, 71 Winter St
 S L Skvirsky, Chestnut Hill, Office Boston, 336 State House
 E C Smith, Brookline, Office Boston 15, 520 Commonwealth Ave
 Kathlyne S Snow, Jamaica Plain, Office Boston 15, 466 Commonwealth Ave
 J W Spellman, Chestnut Hill, Office Brookline 46, 1101 Beacon St
 M H Spellman, Jamaica Plain, Office Boston 15, 475 Commonwealth Ave
 A R Stagg, Medford, 25 Pleasant St
 J P Treanor, Jr, Jamaica Plain, Office Brookline 46, 1101 Beacon St
 W J Walton, Dorchester, 106 Bowdoin St
 N A Welch, West Roxbury, Office Boston 15, 520 Commonwealth Ave, Assistant Treasurer
 P R Withington, Milton 86, 350 Randolph Ave
 Louis Wolff, Brookline, Office Boston 16, 270 Commonwealth Ave
 E T Wyman, Brookline, Office Boston 15, 319 Longwood Ave

NORFOLK SOUTH

D L Belding, Hingham, Office Boston 18, 80 East Concord St, V P, Leg C
 T A Bartlett, Wollaston 90, 308 Beale St. (interim appointment)
 Harry Braverman, Quincy 69, 43 School St
 W R Helfrich, Quincy 69, 166 Washington St
 Frederick Hinchliffe, Cohasset, 117 South Main St, A M N C
 E K Jenkins, South Braintree 85, Norfolk County Hospital, Sec
 N R Pillsbury, South Braintree 85, Norfolk County Hospital, A E C
 D B Reardon, Quincy 69, 1186 Hancock St, E. C, M N C
 H A Robinson, Hingham, 205 North St, P R C
 R G Vinal, Norwell, Main St

PLYMOUTH

W H Pulsifer, Whitman, 26 Park Ave, V P
 J C Angley, Bryantville, School St
 A L Duncombe, Brockton, 38 Winthrop St, A E C, A M N C, Leg C
 H H Hamilton, Plymouth, 70 Court St
 P H Leavitt, Brockton, 129 West Elm St
 C D McCann, Brockton, 12 Cottage St, P R C
 R C McLeod, Brockton, Goddard Hospital, Sec
 G A Moore, Brockton, 167 Newbury St, E C
 B H Pearce, South Hanson, Plymouth County Hospital, M N C
 E L Perry, Middleboro, 39 Oak St

SUFFOLK

C C Lund, Boston 15, 20 Gloucester St, V P
 H L Albright, Boston 15, 412 Beacon St
 A W Allen, Boston 16, 266 Beacon St, C
 J W Bartol, Boston, 1 Chestnut St, Ex-Pres
 W H Blanchard, Chelsea 50, Soldiers' Home
 W J Brickley, Boston 15, 274 Boylston St
 W E Browne, Boston 15, 587 Beacon St, Leg C
 A M Butler, Boston 14, Massachusetts General Hospital
 A J A. Campbell, Boston 15, 520 Commonwealth Ave, E C
 David Cheever, Boston 16, 193 Marlborough St
 J F Conlin, Boston, 121 Park Drive
 Pasquale Costanza, East Boston 28, 238 Maverick St
 N W Faxon, Boston 14, Massachusetts General Hospital
 Jacob Fine, Boston 15, 330 Brookline Ave
 Reginald Fitz, Boston 15, 319 Longwood Ave, Ex-Pres
 Maurice Fremont-Smith, Boston 15, 12 Hereford St
 Channing Frothingham, Boston, Office Jamaica Plain 30, 1153 Centre St, Ex-Pres
 Joseph Garland, Boston 16, 266 Beacon St
 R L Goodale, Boston 16, 330 Dartmouth St, Sec
 A P Heusner, Boston 18, 818 Harrison Ave
 John Homans, Boston 16, 311 Beacon St
 A A Hornor, Boston 15, 319 Longwood Ave, M N C, P R C
 L M Hurxthal, Boston 15, 605 Commonwealth Ave
 C S Keefer, Boston 18, 65 East Newton St
 H A Kelly, Winthrop 52, 200 Pleasant St
 T H Lanman, Boston 15, 300 Longwood Ave
 R I Lee, Boston 16, 264 Beacon St, Ex-Pres
 Donald Munro, Boston 18, 818 Harrison Ave
 R N Nye, Boston 15, 8 Fenway
 F R Ober, Boston 16, 234 Marlborough St, Ex-Pres
 F W O'Brien, Boston 15, 465 Beacon St
 J P O'Hare, Boston 15, 520 Commonwealth Ave
 L E Parkins, Boston 15, 12 Bay State Rd
 L E Phaneuf, Boston 16, 270 Commonwealth Ave
 Helen S Pittman, Boston 16, 264 Beacon St
 J H Pratt, Boston 11, 30 Bennet St
 W H Robey, Boston 16, 202 Commonwealth Ave, Ex-Pres
 H F Root, Boston 15, 81 Bay State Rd, A E C
 R M Smith, Boston 16, 330 Dartmouth St, C
 M C Sosman, Boston 15, 721 Huntington Ave
 Augustus Thorndike, Boston 15, 319 Longwood Ave
 J J Todd, Boston 15, 587 Beacon St
 S N Vose, Boston 15, 29 Bay State Rd

MPHIRE — *President*, John J. Curran, Northampton, *resident*, Edward J. Manwell, Northampton, *secretary*, Mary P. Snook, Worthington, *librarian*, M. O'Keefe, Northampton, *executive counselor*, Henry adgell, Belchertown, *legislative counselor*, Lawrence N. id, Amherst, *public-relations counselor*, Joseph R. as, Williamsburg

MIDDLESEX EAST — *President*, Walter H. Flanders, Melrose, *vice-president*, Daniel L. Joyce, Woburn, *secretary*, Roy Layton, Melrose, *treasurer*, Albert E. Small, Melrose, *librarian*, Angelo L. Maetta, Winchester, *executive counselor*, Kenneth L. Macdachlan, Melrose, *legislative counselor*, M. Wilcox, Woburn, *public-relations counselor*, Milton Quinn, Winchester

MIDDLESEX NORTH — *President*, William F. Ryan, Lowell, *vice-president*, C. Stoyke Baker, Lowell, *secretary*, Brendan D. hey, Lowell, *treasurer*, Mason D. Bryant, Lowell, *executive counselor*, William F. Ryan, Lowell, *legislative counselor*, Harold R. Gardner, Lowell, *public-relations counselor*, Mel J. Ellison, Lowell

MIDDLESEX SOUTH — *President*, John F. Casey, Allston, *vice-president*, Arthur M. Jackson, Everett, *secretary*, Alexander A. Levi, Newton Centre, *treasurer*, Fahyan Packard, Belmont, *orator*, Harold E. MacMahon, Cambridge, *executive counselor*, Harold G. Giddings, Newton Centre, *legislative counselor*, Kenneth J. Tillotson, Belmont, *public-relations counselor*, Gordon M. Morrison, Waban

NORFOLK — *President*, John H. Cauley, Dorchester, *vice-president*, Carl Bearse, Newton, *secretary*, Basil E. Barton, West Roxbury, *treasurer*, Frederick Reis, Jamaica Plain, *executive counselor*, Charles J. Kickham, Brookline, *public-relations counselor*, Dean S. Luce, Canton

NORFOLK SOUTH — *President*, David L. Belding, Hingham, *vice-president*, Robert L. Cook, Quincy, *secretary and librarian*, Ebenezer K. Jenkins, Braintree, *treasurer*, Francis G. King, North Quincy, *executive counselor*, Daniel B. Reardon, Quincy, *legislative counselor*, David L. Belding, Hingham, *public-relations counselor*, Henry A. Robinson, Hingham

PLYMOUTH — *President*, Walter H. Pulsider, Whitman, *vice-president*, Frank E. Wheatley, Brockton, *secretary*, Ralph C. McLeod, Brockton, *treasurer*, Alton L. Hurlhurt, East Bridgewater, *librarian*, John H. Weller, State Farm, *executive counselor*, George A. Moore, Brockton, *legislative counselor*, Alfred L. Duncombe, Brockton, *public-relations counselor*, Charles D. McCann, Brockton

SUFFOLK — *President*, Charles C. Lund, Boston, *vice-president*, Hollis L. Alhright, Boston, *secretary*, Robert L. Goodale, Boston, *treasurer*, Richard S. Eustus, Boston, *executive counselor*, Alexander J. A. Campbell, Boston, *legislative counselor*, William E. Browne, Boston, *public-relations counselor*, Albert A. Hornor, Boston

WORCESTER — *President*, Lester M. Felton, Worcester, *vice-president*, Frank B. Carr, Worcester, *secretary*, Julius J. Tegelberg, Worcester, *treasurer*, Edward P. Disbrow, Worcester, *librarian*, John Fallon, Worcester, *executive counselor*, Bancroft C. Wheeler, Worcester, *legislative counselor*, George R. Dunlop, Worcester, *public-relations counselor*, Nicholas S. Scarcello, Worcester

WORCESTER NORTH — *President*, Rudolf F. Bachmann, Fitchburg, *vice-president*, Francis A. Reynolds, Athol, *secretary*, James G. Simmons, Fitchburg, *treasurer*, Frederick H. Thompson, Jr., Fitchburg, *executive counselor*, C. Bertram Gav, Fitchburg, *legislative counselor*, John J. Curley, Leominster, *public-relations counselor*, James V. McHugh, Leominster

ADMISSIONS RECORDED FROM MAY 23, 1945, TO MAY 22, 1946

YEAR OF ADMISSION	NAME AND RESIDENCE	MEDICAL SCHOOL
1946	*Abrams, Sidney Martin, Malden	Middlesex
1946	Abodeely, Robert Assad, Worcester	Boston University
1946	Achin, Joffre Victor, Charlton City	Tufts
1946	Allen, Roger Everett, Shrewsbury	Tufts
1946	*Andaloro, Vincent A., Everett	Middlesex
1946	Anderson, Fred A., West Roxbury	Boston University
1945	Anderson, John Clifford, Stoneham	Tufts
1945	Angelo, Peter, Waltham	Tufts
1945	Antonellis, Carl Joseph, Cambridge	Tufts
1946	Appleford, George Burton, Springfield	Tufts
1946	Aphaga, Bromie John Peter, Brighton	Tufts
1945	*Arakelian, Michael John, Methuen	Kansas City University of Physicians and Surgeons
1945	Arbeene, George Norman, Somerville	Tufts
1945	Ascher, David Samuel, Brighton	Tufts
1945	Astwood, Edwin Bennett, Brookline	McGill University
1946	*Atwood, Eldridge Delories, Woburn	College of Physicians and Surgeons, Boston
1946	Austen, George, Jr., Brookline	Harvard
1946	Awramik, Stanley Maryan, Lynn	Boston University
1945	Bacon, William Benjamin, Brookline	Harvard
1946	Baker, William Jessamin, Cambridge	Harvard
1946	Balboni, Victor G., Boston	Harvard
1945	*Bannerman, Donald Bruce, East Bridgewater	Middlesex
1946	*Barbieri, Joseph Gene, Lawrence	Middlesex
1945	*Barrette, Repe A., Fall River	College of Physicians and Surgeons, Boston
1945	Bellinger, Martin John, Boston	Harvard
1946	Bengloff, Harold, Brookline	Harvard
1946	Bennett, Robert Edward, Worcester	Tufts
1946	*Benson, William, Lynn	Middlesex
1946	Berg, Milton Louis, Everett	Harvard
1946	Berry, Francis Leonard, Milford	Tufts
1945	Bilodeau, Charles Cloudman, Longmeadow	Columbia University
1946	Binder, Eugene Norman, Chestnut Hill	Boston University
1946	Blanchard, Herbert Norman, Hingham	Boston University
1946	*Blank, Joseph George, Waltham	Middlesex
1945	*Blesoff, Benjamin, Somerville	Middlesex
1946	Block, Herman Leonard, Roxbury	Boston University
1945	Blodgett, James Thomas, West Boylston	Harvard
1946	Bloomberg, John Hollis, Chestnut Hill	Tufts
1946	Bluhm, Samuel, Dorchester	Tufts
1946	Bolduc, Robert Aime, Worcester	Tufts
1945	Botsford, Thomas Winston, Boston	Harvard

SUFFOLK

J H Pratt, Boston, *supervisor*
H T Hutchins, Boston
A J A. Campbell, Boston
W E Browne, Boston
L M Hurxthal, Boston

WORCESTER

B C Wheeler, Worcester, *supervisor*
J W McKoan, Jr., Worcester
H K Spangler, Worcester
E J Crane, Holden
J B Butts, Worcester

WORCESTER NORTH

C B Gay, Fitchburg, *supervisor*
G P Keaveny, Fitchburg
J W Mason, Ashburnham
E B Hopkins, Ayer
W E Currier, Leominster

VICE-PRESIDENTS OF THE MASSACHUSETTS MEDICAL SOCIETY (*Ex-Officio*) FOR 1946-1947

PRESIDENTS OF DISTRICT MEDICAL SOCIETIES

(Arranged according to seniority of fellowship in the Massachusetts Medical Society)

ESSEX SOUTH — Charles A Worthen, Lynn
PLYMOUTH — Walter H Pulsifer, Whitman
MIDDLESEX SOUTH — John F Casey, Boston
MIDDLESEX NORTH — William F Ryan, Lowell
NORFOLK SOUTH — David L Belding, Boston
SUFFOLK — Charles C Lund, Boston
ESSEX NORTH — Guy L Richardson, Haverhill
BRISTOL SOUTH — Salmon P Wilde, New Bedford
WORCESTER — Lester M Felton, Worcester
BERKSHIRE — N Newall Copeland, Pittsfield
BRISTOL NORTH — William M Stobbs, Attleboro
HAMPSHIRE — Adolph Franz, Jr., Holyoke
BARNSTABLE — Harold F Rowley, Harwich Port
WORCESTER NORTH — Rudolf F Bachmann, Fitchburg
FRANKLIN — John B Temple, Shelburne Falls
HAMPSHIRE — John J Curran, Northampton
NORFOLK — John H Cauley, Dorchester
MIDDLESEX EAST — Walter H Flanders, Melrose

COMMISSIONERS OF TRIAL FOR 1946-1947

BARNSTABLE — F O Cass, Provincetown
BERKSHIRE — J B Thomas, Pittsfield
BRISTOL NORTH — J W Cook, Mansfield
BRISTOL SOUTH — A C Lewis, Fall River
ESSEX NORTH — F W Anthony, Haverhill
ESSEX SOUTH — O C Blair, Lynn
FRANKLIN — K W D Jacobus, Turners Falls
HAMPSHIRE — F K Dutton, Springfield
HAMPSHIRE — W M Dobson, Northampton
MIDDLESEX EAST — I W Richardson, Wakefield
MIDDLESEX NORTH — J F Boyle, Lowell
MIDDLESEX SOUTH — H P Stevens, Cambridge
NORFOLK — W J Walton, Dorchester
NORFOLK SOUTH — F A Bartlett, Wollaston
PLYMOUTH — J A Carriulo, Brockton
SUFFOLK — J R Torbert, Boston
WORCESTER — W P Bowers, Clinton
WORCESTER NORTH — H C Arcy, Gardner

OFFICERS OF THE SECTIONS FOR 1946-1947

SECTION OF MEDICINE

Chairman, Daniel J Ellison, Lowell, *vice-chairman*, Francis C Hall, Boston, *secretary*, Laurence B Ellis, Boston

SECTION OF SURGERY

Chairman, Alexander J A Campbell, Boston, *secretary*, George Reynolds, Pittsfield
Executive Committee — E Parker Hayden, Boston, Charles C Lund, Boston, Edward L Pearson, Salem

SECTION OF PEDIATRICS

President, Hyman Green, Boston, *secretary*, Gerald N Hoeffel, Boston and Cambridge
Executive Committee Chairman, James Marvin Bittell, Belmont and Brookline, Leroy T Stokes, Haverhill, Floyd R Smith, Pittsfield

SECTION OF OBSTETRICS AND GYNECOLOGY

Chairman, William J McDonald, Boston, *vice-chairman*, Arthur T Hertig, Boston, *secretary*, George Van S Smith, Brookline

SECTION OF RADIOLOGY

Chairman, Edward B D Neuhauser, Cambridge and Boston, *secretary*, Hugh F Hare, Newton and Boston

SECTION OF PHYSIOTHERAPY

Chairman, William D McFee, Haverhill, *secretary*, Henry A Taddell, Belchertown

SECTION OF DERMATOLOGY AND SYPHILOLOGY

Chairman, Jacob Swartz, Brookline, *secretary*, Francis Thurmon, Boston

SECTION OF ANESTHESIOLOGY

Chairman, Sidney C Wiggan, Waban, *secretary*, Morris J Nicholson, Boston

OFFICERS OF THE DISTRICT MEDICAL SOCIETIES FOR 1946-1947

BARNSTABLE — *President*, Harold F Rowley, Harwich Port, *vice-president*, Arthur J D'Elia, Harwich Port, *secretary*, Oscar S Simpson, Centerville, *treasurer*, Frank Travett, Barnstable, *librarian*, Sheldon L Hunt, Yarmouth Port, *executive counselor*, Paul M Butterfield, Harwich, *public relations counselor*, Paul P Henson, Hyannis

BERKSHIRE — *President*, N Newall Copeland, Pittsfield, *vice-president*, Modestino Criscitello, Pittsfield, *secretary*, Daniel N Beers, Pittsfield, *treasurer*, Theodore W Jones, Pittsfield, *executive counselor*, Isaac S F Dodd, Pittsfield, *legislative counselor*, John Hughes, Pittsfield, *public relations counselor*, Patrick J Sullivan, Dalton

BRISTOL NORTH — *President*, William M Stobbs, Attleboro, *vice-president*, Joseph V Chatigny, Taunton, *secretary*, William J Morse, Attleboro, *treasurer*, Charles E Hoye, Taunton, *executive counselor*, Joseph L Murphy, Taunton, *legislative counselor*, Curtis B Kingsbury, Taunton, *public-relations counselor*, Milton E Johnson, Attleboro

BRISTOL SOUTH — *President*, S Perry Wilde, New Bedford, *vice-president*, George W Blood, Fall River, *secretary and treasurer*, James E Fell, Fall River, *executive counselor*, Richard B Butler, Fall River, *legislative counselor*, Curtis C Tripp, New Bedford, *public-relations counselor*, Harold E Perry, New Bedford

ESSEX NORTH — *President*, Guy L Richardson, Haverhill, *vice-president*, Lincoln C Peirce, Newburyport, *secretary*, Harold R Kurth, Methuen, *treasurer*, J LeRoy Wood, Methuen, *executive counselor*, Rolf C Norris, Methuen, *legislative counselor*, Nicandro F DeCesare, Methuen, *public relations counselor*, Harold R Kurth, Methuen

ESSEX SOUTH — *President*, Charles A Worthen, Lynn, *vice-president*, Hubert A Boyle, Middleton, *secretary*, Henry D Stebbins, Marblehead, *treasurer*, Andrew Nichols, Jr., Danvers, *executive counselor*, Walter G Phippen, Salem, *public-relations counselor*, Loring Grimes, Swampscott.

FRANKLIN — *President*, John B Temple, Shelburne Falls, *vice-president*, Lawrence R Dame, Greenfield, *secretary and treasurer*, Harry L Craft, Ashfield, *executive counselor*, John E Moran, Greenfield, *legislative counselor*, Arthur W Hayes, Greenfield, *public-relations counselor*, Frank A Millett, Greenfield

HAMPSHIRE — *President*, Adolph Franz, Jr., Holyoke, *vice-president*, Arthur F G Edgelow, Springfield, *secretary and treasurer*, George C Steele, West Springfield, *executive counselor*, William A R Chapin, Springfield, *legislative counselor*, Arthur H Riordan, Indian Orchard, *public-relations counselor*, Patrick E Gear, Holyoke

5	Halpin, William Joseph, Medford	Tufts
6	*Hamburger, Herbert, Worcester	University of Pisa
6	Hamlin, Hannibal, Weston	Yale
6	*Hannon, Harland N., North Grafton	Kansas City University of Physicians and Surgeons
5	Hardy, Irad Benjamin, Jr., Waltham	Harvard
5	*Hauck, Charles Wilfred, Brookline	Middlesex
6	Heath, Wilmer Porter, Needham	Boston University
6	Heels, William Garland, North Adams	Harvard
46	Hogan, Edward Norbert, Dorchester	Georgetown University
45	Hogan, Gerald Francis, Amherst	Tufts
46	Hunt, Richard Joseph, Stoneham	Tufts
46	*Hyfer, Harry Jack, Winthrop	Middlesex
46	Isenstein, Charles, Brookline	Tufts
45	*Jacobs, Ezra Astor, Brookline	College of Physicians and Surgeons, Boston
46	*Jellinek, Kurt, Middleboro	University of Vienna
46	Joel, Samuel W., Belmont	Tufts
46	Johnson, Elwood Gordon, Waltham	Tufts
46	Johnson, Goodwin Adolph, Brookline	Tufts
46	Kane, Francis Clement, Salem	Middlesex
46	*Karp, Isadore Albert, Chelsea	Middlesex
46	*Karp, Lewis S., Worcester	Boston University
46	Kaufman, Sumner, Chelsea	Rush Medical College
46	Kaufmann, Gustav Grosvenor, Andover	Tufts
46	Keenan, George Francis, West Roxbury	Tufts
46	Kibbe, Milton Homer, West Springfield	University of Pennsylvania
46	Kirsh, David, Boston	Tufts
46	Klein, Leonard Milton, Roxbury	Tufts
46	Knox, Barron D., Springfield	Tufts
445	Koenig, Emil John, Jr., Holden	University of Bologna
445	*Kraus, Paul Stefan, North Grafton	University of Munich
446	*Kretzmer, Eugene, Worcester	Boston University
445	Lamphier, Timothy Andre, Wellesley Hills	Harvard
446	Landsteiner, Ernest Karl, Newton Centre	Tufts
445	Lapidus, Bernard, Dorchester	Tufts
446	Leary, Howard Leo, Jamaica Plain	Yale
445	Leonard, John Charles, Melrose	Harvard
446	Levenson, Stanley Mortimer, Boston	Harvard
446	Levine, Harold David, Brookline	Middlesex
446	*Levine, Louis, New Bedford	Tufts
446	Levine, Saul Charles, Malden	University of Michigan
446	Lewis, Donald King, Winchester	Harvard
445	Linenthal, Arthur Joseph, Brookline	University of Naples
446	*Litton, Nina, Brookline	University of Virginia
445	Livingston, Stanton Knowlton, West Roxbury	Middlesex
446	*London, Clarence, Lynn	University of Pennsylvania
445	Mahaney, William F., Norwood	Middlesex
446	*Mandrachia, Alfonso Charles, Everett	Tufts
446	Martinson, Melvin Stanley, Acton	Harvard
446	Matson, Donald Darrow, Boston	Georgetown University
445	McAuliffe, Eugene Francis, Jr., Boston	Georgetown University
445	McCann, John Buckley, Brockton	Middlesex
446	*McCarthy, Allan Joseph, Arlington	Harvard
446	McCarthy, Thomas Francis, Lowell	Hahnemann Medical College
445	McCormack, George Augustine, Medford	University of Wisconsin
446	McDonough, Francis Edward, West Newton	Tufts
445	McDonough, James Francis, Woburn	Chicago Medical School
446	*McKerr, Frederick Gunby, Pittsfield	Harvard
446	Mead, Sedgwick, Littleton	Tufts
446	Michaud, Gerard Norman, Salem	Middlesex
445	*Mighore, Joseph O., Malden	Middlesex
446	*Mills, Arnold, Mattapan	Tufts
446	Milner, Leo Robert, Brookline	New York University
446	Miner, Theodore Richardson, Longmeadow	Tufts
446	Moran, Richard James, Arlington	Boston University
445	Mousselet, Mabel Weaver, Boston	Tufts
446	Mulcahy, Richard Edward, Uxbridge	Mid-West Medical College
445	*Murphy, John Patrick, Jamaica Plain	New York University
446	Murray, Martin B., Springfield	Wayne University
445	Nadas, Alexander S., Greenfield	St. Louis University
446	Nash, William Cornelius, Lynn	Tufts
445	Neber, Jacob, Newton Centre	Middlesex
445	*Nichols, Charles Irving, Medford	Middlesex
446	*Noonan, John Philip, Brockton	University of Vienna
445	*Nussbaum, Julius, Lynn	Jefferson Medical College
446	Oliver, Howard Murray, Worcester	College of Physicians and Surgeons, Boston
446	*Olson, John Herbert, Colrain	Harvard
446	Palmer, Edward Joseph, Lexington	Middlesex
446	*Parton, George Povey, Jr., Wellesley	Tufts
445	Peabody, Stephen Davis, Newburyport	Harvard
446	Pearson, Robert Winsor, Beverly	University of Vermont
446	Pekala, Stanley John, Pittsfield	Kansas City University of Physicians and Surgeons
446	*Pinzino, Charles James, Brockton	

1946	Bourgeois, George Albert, Boston	Tufts
1945	Braconier, Harry Erland, Belmont	Tufts
1946	Bragan, James A., Swampscott	Tufts
1946	Brown, Albert Abraham, Lynn	Boston University
1945	Brown, Ralph E., Jr., Waltham	Tufts
1946	Bryer, James Allen, Jr., North Attleboro	Tufts
1945	*Burian, Hermann Martin, Newton Highlands	University of Belgrade
1945	Bush, Cecelia Agnes O'Farrell, Brighton	Tufts
1946	*Campbell, Donald E., Stockbridge	Middlesex
1946	Capodice, Florindo Horace, Dorchester	Boston University
1946	Carleton, William Talbot, Worcester	Harvard
1946	Cartwright, John Thompson, Randolph	University of Pennsylvania
1946	Cass, Victoria Maxwell, Winchester	Tufts
1946	*Castleton, Herbert Edward, Rockland	Middlesex
1945	*Cerrato, Calvin Michele, Cambridge	University of Bologna
1946	*Cinella, John Thomas, Lee	Middlesex
1945	Clark, Glenmore Ford, North Andover	Medico-Chirurgical College (Philadelphia, Pa.)
1946	Clough, Joseph Messer, Boston	Jefferson Medical College
1945	Cloyes, Lorraine, West Newbury	Boston University
1946	Cohen, Manley B., Dorchester	Laval University
1946	Compton, David Wesley, Boston	University of Pennsylvania
1945	Connors, John Phillip, Worcester	Georgetown University
1946	*Cotter, John Thomas, North Attleboro	College of Physicians and Surgeons, Boston
1946	Cotter, Joseph Robert, Newton Upper Falls	Tufts
1946	*Covner, Philip David, Lynn	Chicago Medical School
1946	Cozza, Lawrence Francis, Medford	Tufts
1945	Crane, Timothy Francis, Cambridge	Columbia University
1945	Creeden, Francis Vincent, Brockton	Georgetown University
1946	Croskery, William Francis, Worcester	Boston University
1946	Currens, James H., Brookline	Duke University
1946	Curtis, Charles Nason, Salem	Tufts
1946	Curtis, Sprague, Springfield	Tufts
1946	*Davis, Albert, Quincy	Middlesex
1945	*DeCesare, Frank J., Methuen	Middlesex
1945	*DeFeo, Amadeo Joseph, Everett	Middlesex
1946	DeMinico, Luigi B., Jamaica Plain	Tufts
1946	Derrick, Charles Campbell, Springfield	University of Chicago
1945	Dorsey, Joseph Farrell, Boston	University of Tennessee
1945	Duston, Charles H., Boston	Tufts
1946	Dyer, Edward Carlton, Brookline	Harvard
1946	Egnatz, Nicholas, Jr., Westfield	Indiana University
1946	Ellis, Daniel Sumner, Cambridge	Harvard
1946	Elton, Norman William, Newton Highlands	Boston University
1945	Espinoza, David Valencia, Boston	Tufts
1946	Eyres, Alfred Ernest, Worcester	Iowa State University
1945	Fagan, Frederick John, Taunton	Boston University
1945	Fagan, John Francis, Jr., Dorchester	George Washington University
1945	Failla, Samuel Di Grandi, Greenfield	University of Georgia
1946	Famiglietti, Joseph Angelo, East Boston	Tufts
1945	Ferrarone, Edward Joseph, Springfield	Georgetown University
1946	Finnell, Ambrose Francis, New Bedford	Georgetown University
1946	Fiore, Autino, Cambridge	Tufts
1945	*Fischer-Galati, Theodore Isidore Max, Andover	University of Vienna
1946	Fisher, Robert Martin, Waltham	Columbia University
1945	Fitzgerald, Edward Francis, Quincy	Georgetown University
1945	Fitzpatrick, Audrey Jane, Worcester	Tufts
1945	Flaschner, Ira, Newton	Boston University
1945	Ford, Frederick Francis, Waltham	Georgetown University
1946	*Friberg, Robert Adolph, Winchester	Middlesex
1946	*Friedland, Fritz, Brookline	University of Berlin
1946	*Frisch, Joseph, Vineyard Haven	Middlesex
1946	*Frogel, Reuben Harry, East Braintree	Middlesex
1946	*Galbo, Samuel Joseph, Shelburne Falls	Middlesex
1945	Ganem, Emil Joseph, Methuen	Johns Hopkins University
1946	*Gaspar, Shari Band, Baldwinville	Royal Hungarian University of Pecs
1946	Gilmore, Raymond, Lowell	Tufts
1946	Ginsburg, Edward Merrill, Quincy	Emory University
1945	Guhano, Charles Edward, Brookline	Baylor University
1946	*Gold, Abraham, Chelsea	Middlesex
1945	*Goldblatt, Harold William, Lawrence	Medical School, Royal Colleges
1946	Golden, Theodore Solomon, Newton	Tufts
1946	*Goldman, Herbert, Lynn	Middlesex
1946	Goodale, Walter Temple, Weston	Harvard
1945	Gorfine, Robert, Allston	St. Louis University
1945	Gould, Louis Nathan, Northampton	New York Medical College
1946	*Green, Max Benjamin, Lawrence	Middlesex
1945	Greenblatt, Milton, Boston	Tufts
1945	Gregory, Elizabeth A., Boston	Boston University
1946	Grendal, Michael Francis, Roslindale	Jefferson Medical College
1946	Guralnick, Eugene, Roxbury	Tufts
1946	Haase, Ferdinand, Jr., Boston	Harvard
1945	Haley, William Thomas, Jr., Boston	Tufts

946	Waskow, Eleanor A , Boston	University of Wisconsin
946	Weinstein, Louis, Brighton	Boston University
946	Weisman, Avery Danto, Boston	University of Michigan
946	Weiss, William Anthony, Boston	Jefferson Medical College
945	Welcker, Merrill Louis, Jr , South Duxbury	Tufts
946	Westmeyer, Marion Wallace, Melrose	College of Medical Evangelists
1945	*White, Edward G , Springfield	Chicago Medical School
1945	Wildberger, William C , West Newton	Boston University
1946	Wilson, Walter E , Jr , Brookline	Emory University
1946	Winograd, Abbott Louis, Lynn	University of Michigan
1946	Wise, Charles Samuel, Cambridge	New York University
1946	Wood, William Baxter, West Roxbury	Tufts
1946	Worthen, Charles Arthur, Jr , Lynn	Tufts
1946	Zeltzman, Israel, Roxbury	Tufts
1946	Zupanec, Ralph, Pittsfield	University of Kansas

Total 302

*The candidate, after a personal interview, was approved by the Committee on Membership and permitted to take an examination before a board of censors

DEATHS REPORTED FROM MAY 23, 1945, TO MAY 22, 1946

ADMITTED	NAME	PLACE OF DEATH	DATE OF DEATH	AGE
1931	Alexandrov, Vitaly John	Rutland	March 5, 1946	55
1933	Anshin, Marcus Moses	Lynn	May 21, 1945	52
1905	Atwater, James Billings	Westfield	May 3, 1946	87
1903	Bartley, John Joseph	Lawrence	June 16, 1945	73
1894	†Baxter, Edward Hooker	Hyde Park	July 30, 1945	93
1914	Bresnahan, Frank Nesdel	Cambridge	July 29, 1945	58
1921	†Brodrick, Francis Sidney	Boston	September 11, 1945	77
1917	Buck, William Edgar	Randolph	September 15, 1945	58
1936	Burgess, Charles James	Lawrence	February 16, 1946	76
1906	Cabot, Hugh	Ellsworth, Maine	August 14, 1945	73
1898	Cannon, Walter Bradford	Franklin, New Hampshire	October 1, 1945	73
1904	Cavanaugh, Mortimer Thomas	Great Barrington	October 7, 1945	73
1925	†Churchill, Frank Spooner	Bass River	February 27, 1946	81
1890	†Consens, Nicholas William	Waltham	March 19, 1946	81
1919	Cox, Oscar Francis	Brookline	June 3, 1945	57
1892	Cox, Oscar Francis	Brookline	June 3, 1945	57
1938	Cox, Oscar Francis	Brookline	June 3, 1945	57
1905	Cregg, Francis Aloysius	Methuen	November 30, 1945	64
1943	Davenport, Benita Coolidge	Middleton	December 20, 1945	57
1932	Davison, Arthur Howard	Milton	September 26, 1945	71
1905	†Dexter, Fred Fay	Springfield	July 10, 1945	66
1898	†Dickson, Richard Ensign	Holyoke	May 8, 1945	77
1888	†Drumme, Nicholas Daniel	Dorchester	December 18, 1945	80
1913	†Edsall, David Linn	Tryon, North Carolina	August 12, 1945	76
1927	Elliott, John Joseph	West Roxbury	March 29, 1946	49
1904	Evans, Miner Harlow Amos	Wellesley Hills	May 5, 1946	65
1919	†Fessenden, Charles Hill	Newton Centre	April 19, 1946	82
1892	†Goodwin, James Joseph	Clinton	December 29, 1945	80
1892	Goray, James Philip	Fitchburg	November 12, 1945	78
1923	Greenway, Major Thomas Herhert, M C , A U S	Framingham	June 23, 1945	44
1896	†Griswold, Merton Lyman	Uxbridge	June 10, 1945	76
1914	Gunter, Fred Clarke	Belmont	April 24, 1946	54
1899	Hammond, William John	East Walpole	July 4, 1945	76
1915	Harkins, William Joseph	Quincy	August 25, 1945	60
1936	Hayes, Captain Paul Thomas, M C , A U S	France	October 1, 1945	36
1915	Hearn, Walter Lawrence	Lynn	September 30, 1945	67
1942	Hurlbut, Lt Robert Satterlee (MC), U S N R	"U S S Halligan off Okinawa"	March 26, 1945	33
1901	Jack, Lewis Harlow	West Newton	May 3, 1946	73
1937	Jacobson, Nathan Louis	Lynn	July 13, 1945	60
1930	Kaplan, Boris	New Bedford	December 25, 1945	56
1935	Keith, Theodore Kent	Newton Centre	January 15, 1946	43
1888	†Lawler, William Patrick	Lowell	December 8, 1945	85
1927	Lee, Frank Robert	North Andover	October 15, 1945	42
1916	Leonard, Edward DeWitt	Newton Centre	December 15, 1945	60
1893	†Libby, Jesse Herbert	Weymouth	September 25, 1945	78
1907	†Lorimer, Felix	Pomona, California	February 23, 1944	79
1907	MacLeod, John Malcolm	Quincy	October 19, 1945	72
1913	†Mayberry, Frank Eugene	Rockland	October 1, 1945	85
1905	McCausland, William James	Quincy	November 5, 1945	70
1904	McLeod, Melvin Saunders	Melrose	February 26, 1946	49
1921				
1942				

1945	Pollen, Abraham, Chelsea	Tufts -
1946	Portman, Harry, Malden	Boston University
1946	Powell, Thurston Gates, Auburndale	Jefferson Medical College
1946	Pratt, Thomas Dennie, Andover	Yale
1946	*Press, Harry Alvin, Pittsfield	Middlesex
1946	*Prochnik, James Jonas, Allston	University of Vienna
1946	Rawson, Rulon Wells, Cambridge	Northwestern University
1946	Reardon, Edward Richard, Worcester	Tufts
1945	*Receptuto, Paul, Somerville	Middlesex
1946	Regan, Francis Clinton, Wellesley	University of Rochester
1945	*Reinisch, Max, Holyoke	University of Prague
1945	*Reyersbach, Gertrud Clara, Boston	University of Göttingen
1946	Richer, Arthur George, Hudson	Tufts
1945	Rini, Joseph, Springfield	Long Island College of Medicine
1945	Rodofsky, Milton Harold, Dorchester	Tufts
1946	Rogell, David, Allston	Tufts
1946	Rogers, Daniel Miner, South Hamilton	Harvard
1945	Roseman, Melvin David, Dorchester	Boston University
1946	*Rosenbaum, Emil Elias, Lowell	University of Berlin
1945	Rosenfeld, Leon, Brookline	Harvard
1946	Ross, Frederick Phelps, Brookline	Harvard
1945	Ross, J. Newton, Brookline	University of Illinois
1945	Ross, John Richard, Needham	Ohio State University
1946	*Rothschild, Alfred F., Worcester	University of Munich
1945	Russo, Edward Atulio, Boston	Tufts
1946	Ryack, Leon, Brookline	New York Medical College
1946	*Saffran, Irving, Mattapan	Middlesex
1945	Sall, Robert Dayton, Mattapan	Harvard
1945	Salwen, Robert, Brookline	Boston University
1946	Scanlon, James Gerald, Worcester	Hahnemann Medical College
1946	*Schechtman, Harold I., Fitchburg	Middlesex
1945	Schier, Woodrow Wilson, Boston	Columbia University
1946	*Schmoyer, Sheron Aaron Alfred, Pittsfield	Middlesex
1946	Schofield, Alan Leslie, Lowell	Tufts
1945	*Schwartz, Harry H., Everett	Middlesex
1946	Schwartz, Isadore, Quincy	Tufts
1946	*Schwartz, Robert, Hyde Park	Middlesex
1946	Sears, Warren Hooper, Springfield	Johns Hopkins University
1945	Secunda, Lazarus, Pittsfield	Columbia University
1945	*Seltzer, Joseph, Newton Centre	Middlesex
1946	Shands, Harley Cecil, Boston	Tulane University
1946	Shapiro, Robert, Brookline	Tufts
1946	Shaughnessy, William Joseph, Worcester	Hahnemann Medical College
1946	Shaw, Lister Harvey, Lowell	Harvard
1946	Shea, Charles Michael, Medford	St. Louis University
1946	Sheddan, Frank G., Jr., Wellesley	Baylor University
1946	*Short, Leonard V., Lexington	Middlesex
1946	Silverman, Irving, Cambridge	Boston University
1945	Simon, Naif Louis, Quincy	Boston University
1945	Smish, Kenneth William, Melrose	Harvard
1945	Smith, Leo Joseph, Dorchester	Tufts
1946	*Sneiderman, Robert, Lynn	Middlesex
1946	Snyder, Philip Frank, Lynn	Tufts
1946	Sommer, Francis Xavier, Newton Centre	Yale
1946	Sorkin, Joseph James, Dorchester	Chicago College of Medicine and Surgery
1946	Spadea, Saveria, Brockton	Loyola University
1945	Squire, Lucy Frank, Boston	Woman's Medical College
1945	*Staffier, Anthony Ralph, West Somerville	Middlesex
1946	Starbuck, George William, Fairhaven	University of Vermont
1946	Stein, Tobias, Boston	Columbia University
1945	Stewart, Donald Mitchell, Malden	Tufts
1946	*Strassmann, George Samuel, Waltham	University of Heidelberg
1946	Stratton, Charles William, Lee	Albany Medical College
1946	Sturdevant, Charles Lyon, Newtonville	University of Nebraska
1946	Sturnick, Melvin Irving, Allston	Tufts
1946	Suzedell, Eugene, Quincy	Boston University
1946	*Sweeney, Guy Raymond, Medford	Middlesex
1945	Swenson, Orvar, Brookline	Harvard
1945	*Tauber, Max, Waltham	Middlesex
1946	*Tedeschi, Pasquale R., Newton	Middlesex
1946	*Thornton, Patrick John Sinclair, Brookline	University of Lausanne
1946	*Turanyi, Bela, Dorchester	Royal Hungarian Elisabeth University
1946	Twigg, Edward James, Winthrop	Tufts
1946	Vanderlaan, Willard Parker, Jr., Marblehead Neck	Harvard
1946	Varnum, Joseph Bradley, Lowell	Tufts
1946	Vassos, George Arthur, Jr., Springfield	Cornell University
1946	Verde, Aldo Guido, Dorchester	Tufts
1945	Walker, George Marshall, Jamaica Plain	Cornell University
1945	*Wantman, Bernard, Somerville	Middlesex
1946	Ware, Paul Francis, Chestnut Hill	Harvard
1945	Warren, George Joseph, Waltham	Tufts
1946	Warren, Joseph Edward, Worcester	Harvard

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

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CASE 32381

PRESENTATION OF CASE

A sixty-four-year-old widow, a railroad clerk, entered the hospital because of unexplained fever.

The patient had apparently been quite well until six weeks before entry, when she developed a painful, patchy erythematous, nonvesicular eruption on the left shoulder posteriorly that persisted for ten days without other symptoms and then disappeared. Following this episode she noted sharp pains and occasional ringing in the left ear. She was treated with a sulfonamide by a physician, and the symptoms cleared without residua. The patient then resumed her work. Three weeks before entry she began to have localized pain and exquisite tenderness in the nares. The area of painful inflammation progressed rapidly, and in two days the malar and nasal aspects of the face were markedly swollen, painful and red. She also developed fever and called her physician, who treated her with a mixture of oral penicillin and Amphogel for four days. Nevertheless, the lesions progressed to involve the eyes, which became red and "bloodshot" and began to burn. The temperature continued, ranging from 100 to 101°F, and was accompanied by a slight headache and anorexia. Two weeks before entry the face involvement had subsided, but the sides and back of the neck, the temporomandibular joints, the occipital region of the scalp and the ears were affected. These areas were hot and red, and in the suboccipital region a small egg-sized mass developed subcutaneously. The condition grew worse until the patient was partially deafened and was awakened nightly by sharp severe pains, especially in the back of the neck, and occasional twinges in both ears. She had lost about 10 pounds during the six weeks before admission.

As an adolescent the patient had had an attack of erysipelas, during which she became quite sick and developed corneal ulcers. Following this illness aching pains in the shoulders had developed. Ten years before entry the patient had spent nine months at a tuberculosis sanatorium because of pleuritic pain in the left chest and weight loss. The tongue had been sore for about two years. Occasional

episodes of urinary frequency, burning and gross hematuria had also occurred during the preceding few years, particularly during the previous six months.

Physical examination revealed a thin woman in no obvious distress, although she complained of tenderness in both temporal regions and along the sternomastoid muscles. The eyes showed old peripheral corneal scars. The ear canals and margins of the drums were somewhat inflamed, particularly on the left. The Weber test was lateralized to the left, and bone conduction was better than air conduction on both sides. The mouth was fissured at the angles, and the tongue was beefy red and sore, with coarse papillae. There was general swelling and slight lymphadenopathy in the region of the left sternomastoid muscle. The lungs were clear, except for a few moist rales at the left base. The heart did not appear enlarged. A blowing systolic murmur was heard at the apex but was not transmitted into the axilla. There was also a soft, blowing systolic murmur over the aortic area. The sounds were regular and of good quality. The abdomen was normal except for slight epigastric tenderness.

The temperature was 101°F, the pulse 100, and the respirations 24. The blood pressure was 160 systolic, 90 diastolic.

Examination of the blood revealed a hemoglobin of 12.5 gm and a white-cell count of 12,600, with 86 per cent neutrophils, 3 per cent lymphocytes, 5 per cent monocytes, 4 per cent eosinophils and 1 per cent basophils. The sedimentation rate was 6 mm in 1 hour. Blood Hinton and Vidal reactions and a brucellergin test were negative, as were five blood cultures. The urine had a specific gravity of 1.014 and showed a ++ test for albumin, the sediment contained 5 red cells and 25 white cells per high-power field.

An x-ray film of the chest showed only irregular areas of calcification about the right hilus and in the right apical region. Examination of the sinuses, a gastrointestinal series and intravenous pyelogram were all negative. A Graham test showed a poorly functioning gall bladder.

The patient was placed on a high-vitamin, high-calorie diet but failed to improve. On the fifth hospital day an episode of urinary frequency and burning, lasting for several hours, occurred. A urine culture was negative, and no acid-fast organisms were seen in a smear. Sulfathiazole was given. On the seventh hospital day a scratchy sound in late midsystole was picked up in the third and the fourth interspace at the left sternal border. Pressure on the bell of the stethoscope brought this sound closer to the ear. The patient was then taken off sulfathiazole and started on salicylates. For the next several days she appeared subjectively improved, although she complained that the deafness was becoming worse. On the tenth hospital day an electrocardiogram was reported to be within normal limits. An

1903	McNamara, John James	Brockton	January 3, 1946	74	
1904	†McPherson, George Edwin	Amherst	June 16, 1945	63	
1914	Metcalf, Richard	Winthrop	May 21, 1945	57	
1912	Metzger, Butler	Lynn	April 25, 1946	71	
1915	Moore, George Andrew	Palmer	October 6, 1945	74	
1921	Morrison, William Henry	Springfield	November 22, 1945	65	
1942	Mulligan, Francis Joseph	Newton	February 3, 1946	44	
1888	†Palmer, Sarah Ellen	Boston	August 23, 1945	Unknown	
1899	†Parker, Ralph Walter	Pelham, New Hampshire	February 18, 1944	67	
1904	†Patterson, Alice Maria	Marblehead	June 20, 1945	75	
1925	Piper, Comdr Frank James (MC), U S N R	Frammingham (on terminal leave)	April 4, 1946	43	
1903	Poirier, Horace	North Conway, New Hampshire	August 14, 1945	67	
1896	†Reddy, Joseph Warren	South Boston	About August 1, 1945	74	
1928	Richardson, Carl Eugene	Franklin	July 30, 1945	61	
1891	†Robbins, Fred Gibson	Salem	May 16, 1945	74	
1911	†Rosenau, Milton Joseph	Chapel Hill, North Carolina	April 9, 1946	77	
1913	Saunders, Edmund Louis	Wilbraham	May 11, 1944	63	
1933	Scenna, Donato Theodore	Melrose (on terminal leave, A U S)	March 3, 1946	41	
1924 } 1938 }	Silbert, Harry	Salem	October 31, 1945	50	
1891 } 1926 }	†Stevens, Harry Lawrence	New Bedford	January 29, 1946	75	
1925	Stratton, Charles William	Lee	November 6, 1945	69	
1906	†Sullivan, Cornelius Augustine	Braintree	March 19, 1946	66	
1928	Talty, Francis Eugene	Hoboken, New Jersey	May 27, 1945	65	
1911	Timmins, Edward Francis	South Boston	December 11, 1945	64	
1894	†Treanor, John Peter	Dorchester	May 4, 1946	81	
1903	Truesdale, Philemon Edwards	Fall River	June 12, 1945	70	
1923	Vance, Michael Edward	Pawtucket, Rhode Island	May 5, 1945	75	
1901 } 1920 }	Warren, Alva Harding	Malden	November 19, 1945	71	
1906	Whelan, Charles	North Cohasset	May 29, 1945	63	
1872	†White, Levi	Worcester	December 1, 1945	96	
1899	Williams, Hugh	Boston	February 22, 1945	72	
1899	†Woods, Charles Edwin	Fitchburg	October 12, 1945	82	
1877	Woodward, Samuel Bayard	Worcester	January 29, 1946	92	
1914 } 1932 }	Worthen, Clarence Field	Boston	August 22, 1945	65	
1939	Wright, Rebekah	Brookline	March 29, 1945	72	
1907	Young, James Herbert	Newton	February 18, 1946	63	
1924	Zielinski, Lt Comdr Ignatius (MC), U S N R	"In a plane crash, near Beacon, N Y "		November 11, 1945	45
	†Retired fellow				

†Retired fellow

Total number of deaths of active fellows	58
Total number of deaths of retired fellows	27
Grand total	85

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Walter G Phippen, M D
Daniel B Reardon, M D
William F Ryan, M D
Henry A Tadgell, M D
Michael A Tighe, M D
Bancroft C Wheeler, M D

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The laboratory findings are of little help. A white-cell count of 13,000 to 30,000 has been noted in lupus erythematosus disseminatus, particularly in the terminal stages of the disease. Leukopenia is thought by some to be a characteristic finding. In our experience, however, it occurs in only about 50 per cent of the cases of disseminated lupus. I have always been struck by the fact that many cases of periarteritis nodosa have a much higher white-cell count than one would anticipate on the basis of the fever.

In summary, I shall say that this was a case of disseminated lupus erythematosus. I shall not be surprised if Dr Mallory reports the finding of vascular lesions that were indistinguishable from those of periarteritis nodosa.

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CLINICAL DIAGNOSIS

Periarteritis nodosa?

Lupus erythematosus?

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Lupus erythematosus disseminatus, with widespread vascular lesions of type seen in periarteritis nodosa.

ANATOMICAL DIAGNOSES

Periarteritis nodosa.

Multiple infarcts of liver and kidneys.

Pericarditis, fibrinous, mild.

Mural thrombus of right auricle.

PATHOLOGICAL DISCUSSION

DR MALLORY: The autopsy in this case showed a pericarditis less marked anatomically than might have been expected from the clinical evidence. The heart was slightly enlarged, weighing 390 gm. The endocardium and valves were normal, but there was a thrombus in the right auricular appendage and a moderate degree of coronary sclerosis, without occlusion in any vessel. The pleural cavities contained 500 cc of fluid on each side, but showed no evidence of inflammation. The liver was quite peculiar. Both the external and the cut surfaces were irregularly mottled with focal dark areas 5 to 10 mm in diameter. In each of these areas the centers of the lobules were large, red and depressed, as in chronic passive congestion. This is the characteristic gross picture of infarction in the liver, which is rarely complete because of the double blood supply and because only those cells in the center of the lobules are killed. The kidneys likewise showed multiple infarcts—in fact, they were so numerous that the picture was suggestive of diffuse cortical necrosis,

erysipeloid lesion about the right ear was again prominent, and penicillin therapy was begun. On the twenty-second hospital day she developed an urticarial rash, which disappeared after penicillin was stopped. Five days later bilateral shoulder pain, with swelling and tenderness on the left, occurred and lasted for three days, being followed successively by a hot, swollen, tender right wrist, a painful, swollen left infrapatellar tendon, a tender left wrist, pain over the scapula region of the back, increased epigastric pain and tenderness with spasm and an attack of numbness in the fingers and thumb of the right hand. The patient continued to suffer from severe malaise, listlessness and anorexia. The pericardial friction rub remained constant. The temperature usually rose to 101° or 102°F in the evening. The white-cell count ranged from 13,000 to 30,000. The sedimentation rate reached 50 mm in 1 hour. Repeated urine examinations showed + or ++ tests for albumin and 5 to 100 red cells per high-power field. Tenderness in the left costovertebral angle was also noted. The patient grew progressively worse. Several transfusions of whole blood brought about only temporary improvement.

On the fifty-second hospital day a pronounced gallop rhythm was heard over the entire precordium. The neck veins became distended. Cyanosis and puffiness of the face were noticeable. Crackling rales were heard at both lung bases. The liver edge was percussed four fingerbreadths below the costal margin. There was slight pitting edema over the sacrum. Nevertheless, the patient was not dyspneic or orthopneic. The pulse was 110, and the blood pressure 175 systolic, 105 diastolic. Repeated blood chemical studies revealed a nonprotein nitrogen of 107 mg and a total protein of 5.9 gm per 100 cc. On the fifty-fourth hospital day, the patient complained of memory loss and pain in the abdomen. The heart was markedly enlarged to percussion, with the point of maximum impulse in the axilla, and a pronounced to-and-fro friction rub was heard over the entire precordium. The urinary output dropped to 60 cc. The patient became stuporous, developed muscular twitching and died on the fifty-eighth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WALTER BAUER: Did the pain arise in the temporomandibular joints or the adjacent muscles?

DR. TRACY B. MALLORY: I do not know.

DR. BAUER: Was it erysipelas or an erysipeloid lesion that developed?

DR. MALLORY: The word "erysipeloid" was used.

DR. BAUER: Was the egg-sized mass a lymph node?

DR. WYMAN RICHARDSON: I saw this patient once but not at that time. I assume that it was a lymph node.

DR. BAUER: I wonder if anyone who saw the patient would be willing to say whether or not the pain followed the course of the arteries.

DR. RICHARDSON: I did not observe it.

DR. BAUER: If I ask any more questions you will know the diagnostic possibilities that I am entertaining.

I interpret the deafness as being of the middle ear type, but more marked on one side. The Weber test as reported does not rule out bilateral nerve deafness. Were urinary cultures and guinea pig inoculations for acid-fast organisms done?

DR. MALLORY: There is no record of such tests.

DR. BAUER: I assume that the beneficial effect of salicylates was short lived.

DR. MALLORY: That is correct.

DR. BAUER: Does anyone know the duration of the circulatory changes described? Were they neurogenic in origin?

DR. RICHARDSON: Again, I must say that I saw the patient before that episode and that I do not know.

DR. BAUER: Will Dr. Lingley show the roentgenograms of the chest and the intravenous pyelograms? I doubt if the gastrointestinal series will be of interest. I assume that the pulmonary findings described were the result of an old acid-fast infection.

DR. JAMES R. LINGLEY: The film of the chest as described shows areas consistent with old tuberculosis of the apex and hilus. The heart is normal. There is evidence of old pleurisy at the left base. On the pyelogram there is excretion from both kidneys, and no abnormalities are demonstrable. On this film the Graham test shows a rather faint shadow.

DR. BAUER: On the basis of this information one wonders if this patient had one or several diseases and when the illness or illnesses began. According to the record, she spent nine months in a tuberculosis sanatorium nine years before admission and was later observed to have pulmonary findings consistent with healed tuberculosis. The genitourinary symptoms, which had been present for at least two years, could have been caused by an acid-fast infection, as the physician in charge suspected. The cutaneous lesions could have been those of erysipelas, and the subsequent serous membrane involvement a manifestation of an ensuing rheumatic fever. Such a sequence of events would account for all the recorded findings. I prefer to reason, however, that the patient suffered from a constitutional disease due to widespread vascular lesions that was first demonstrated by renal involvement. Perhaps I reason this way because of my interest in a special group of diseases. The second manifestation of this patient's illness — the appearance of cutaneous lesions, first over the posterior aspect of one shoulder and later involving the face and neck — is in accord with this concept. Such cutaneous lesions are seen in both disseminated lupus erythematosus and dermatomyositis, but more frequently in the former. Whether the muscles of the face and neck were involved is difficult to

ascertain from the clinical record. At the time of admission the patient had fever, and there was evidence of serous-membrane involvement. Subsequently she developed a migratory arthritis involving a number of articulations and experienced recurring attacks of abdominal pain. This train of events is readily accounted for on the basis of a disease characterized by widespread vascular lesions, such as lupus erythematosus disseminatus, dermatomyositis or periarteritis nodosa. The choice of the proper diagnosis is always difficult, because experience has shown that there may be much overlapping of both clinical and pathological findings in cases of this type. During the last ten years we have seen a number of patients with clinical findings not unlike those observed in the case under discussion. In each case the clinical diagnosis of lupus erythematosus disseminatus was agreed to by Dr. Mallory on the basis of the pathological examination. The exact cause of the cardiac enlargement, which was observed during the last days of the patient's life, is difficult to establish. It could have been a pericardial effusion, diffuse cardiac enlargement or right-sided cardiac enlargement secondary to periarteritis nodosa of the pulmonary vascular system. Such enlargement has been observed in lupus erythematosus disseminatus. I cannot prove its presence in this case, but it is a good possibility.

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although the process was a little too spotty and there were some uninvolved areas. The spleen was grossly normal. On the basis of the multiple areas of infarction in the liver and the kidney it seemed to me that a diagnosis of periarteritis nodosa was inevitable.

When the microscopic sections came through we found vascular lesions in many areas. There was rather marked involvement of the bronchial arteries, although the patient had never had any pulmonary symptoms. Many vessels in the liver and the spleen and the kidney showed lesions of various ages and character. In some the process seemed to be primarily endarteritis, in others occlusive thrombosis, and in a few areas typical periarteritis nodosa, with necrosis of the media, aneurysm formation and so forth. One section from the deltoid muscle showed a typical periarteritic lesion. There was nothing in the case that particularly indicated a diagnosis of lupus, although there was periarterial fibrosis in the spleen, which is consistent with it. The kidney lesions were not suggestive. In several sections from the brain we were unable to find arterial lesions.

DR BAUER: Did the patient ever exhibit jaundice?

DR MALLORY: It was never noticed.

DR RICHARDSON: What do you think of the relation of sulfonamide therapy to this picture?

DR BAUER: I do not know. So far as one can judge from the record the first erythematous lesions appeared prior to sulfonamide therapy. On the basis of past experience and recent experimental studies I should not administer sulfonamides to a patient suspected of having widespread vascular disease of the type mentioned. Whether sulfonamides were a cause in this case, I cannot say.

DR RICHARDSON: You do not believe that they were a cause?

DR BAUER: No, for the reasons previously mentioned.

This case, like others we have seen, illustrates the difficulties the clinician may have in making an accurate anatomical diagnosis. We have seen patients in this hospital who presented the classic textbook picture of disseminated lupus, and yet Dr Mallory made a diagnosis of periarteritis nodosa on the basis of the microscopic findings. The onset of the disease in this patient resembled both disseminated lupus and dermatomyositis. The subsequent course was more like that of disseminated lupus or periarteritis nodosa. Was this another overlapping case of the type mentioned? I know of no similar case of periarteritis nodosa on record, although Keil* reported the appearance of a red, painful, cutaneous lesion as the first manifestation of the disease in 1 case. Can it be that these diseases, which simulate one another so closely, represent different manifestations of a common pathogenesis? Have you ever seen a case like this, Dr Ropes?

DR MARIAN ROPES: No.

DR MALLORY: There is no evidence to add from

the anatomical point of view. There was a wide variety of vascular lesions, some acute, some certainly of months' duration, and some possibly going back two years, although I cannot say that definitely.

CASE 32382

PRESENTATION OF CASE

A seventy-one-year-old retired shoe laster entered the hospital because of bloody urine.

Seven years before entry the patient had had an attack of acute urinary retention, and a suprapubic prostatectomy had been performed at another hospital, following which intermittent painless hematuria and the occasional passage of small blood clots had begun. A year later, cystoscopy was performed at the same hospital and a section of tissue removed from a "growth in the bladder." This procedure effected marked improvement, although the urine continued to be occasionally bloody. Three months before entry almost daily hematuria suddenly began, with frequent passage of clots. Two months later cystoscopy in the Out Patient Department disclosed no source of the bleeding. An intravenous pyelogram showed an enlarged left kidney that failed to excrete the dye during the twenty-minute observation period, the right kidney appeared normal. The bones of the pelvis showed a coarse trabeculation and thickening of the cortex. Shortly thereafter the patient had an episode of urinary retention and was kept on constant drainage at the other hospital for four days. He also developed chills, nausea, vomiting and pain in the left flank and lost 10 pounds in weight. These symptoms persisted. Three days before entry the patient was again cystoscoped in the Out Patient Department, and bright-red blood was seen to come from the left ureter even when the catheter was inserted up to 25 cm. Considerable reddening and some small nubbins-like projections were found about the left ureteral orifice. A retrograde pyelogram did not give satisfactory filling of the left kidney pelvis. The kidney calyces appeared enlarged, and there was a suggestion of a rather large, smooth, filling defect against the neck of the upper calyx and the pelvis. The kidney outline was not clearly seen on any of the films.

Physical examination on admission revealed an increase in the anteroposterior diameter of the chest, as well as poor expansion. The heart was normal. A large, warm, tender mass, with a somewhat softer center than normal, was present at the left costovertebral angle and extended into the left flank. The entire left side of the abdomen was moderately tense and tender. The liver appeared to be somewhat enlarged.

The temperature, pulse and respirations were normal. The blood pressure was 135 systolic 80 diastolic.

Examination of the blood revealed a hemoglobin of 75 per cent and a white-cell count of 10,600.

*Keil, H. Conception of lupus erythematosus and its morphologic variants, with particular reference to 'systemic' lupus erythematosus. *Arch. Dermat. & Syph.* 36: 729-757, 1937.

The urine, which was amber colored and acid, had a specific gravity of 1.012 and gave a +++ test for albumin. The sediment contained 250 red cells and 250 white cells, with many clumps, per high-power field. Culture revealed abundant colon bacilli. X-ray examination of the chest was negative. A biopsy of the bladder was reported as showing malakoplakia.

During the first week in the hospital the mass in the left costovertebral angle became larger, warmer and definitely fluctuant in several places, although the patient had no fever and only a slight leukocytosis. Aspiration produced 4 cc of brownish pus that showed a slight growth of colon bacilli and aerobic gram-positive bacilli.

On the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. FIORINDO A. SIMEONE This patient had had painless hematuria for seven years, but the presenting symptoms when he was admitted to the hospital were chills, nausea, vomiting, pain in the left flank and weight loss. The physical examination showed the usual signs of inflammation in the left flank. In addition, brownish pus was aspirated from the mass in the flank. A diagnosis of perinephric abscess can therefore be made without much question. Incidentally, the physical examination and x-ray studies suggest that there was no gross lesion other than that in the genitourinary tract. The slight enlargement of the liver was probably of no significance. The heart and lungs were normal on x-ray and physical examination. The peripheral edema could have been the result of malnutrition during the month or more prior to admission, and it could have been associated with hypoproteinemia caused by the loss of blood and protein in the urine during the long period of illness.

Patients with perinephric abscesses can be classified in two main groups — simple and complicated. The distinction is important because both etiology and prognosis are different in the two groups. Simple perinephric abscess is the type secondary to metastasis of organisms from foci of infections elsewhere, such as carbuncles, furuncles and severe tonsillitis. The usual organism is *Staphylococcus aureus* or the streptococcus. The complicated type, which has a relatively poor prognosis, is encountered in patients who, as a rule, have had long-standing infection in the kidney that has spread through the renal parenchyma and into the perinephric space. Later, such infection may actually perforate Gerota's capsule and point in the costovertebral angle. The symptoms and signs recorded in the history of this case are consistent with a diagnosis of complicated perinephric abscess. The patient had gross infection in the left kidney, as manifested by the presence of red cells and large numbers of white cells in the urine and by the culture of colon bacilli — presumably the same organism cultured from the

pus aspirated from the flank. No function could be demonstrated in the left kidney by excretory roentgenography.

What was the cause of the pyelonephritis in this case? Seven years before admission a suprapubic prostatectomy had been performed after acute urinary retention that was presumably caused by benign hypertrophy of the prostate. It is possible, on the other hand, that the retention developed because of the presence of blood clot or tissue fragments in the bladder. These could have arisen from a malignant tumor of the kidney or ureter, but there is no information to help settle the question and it should be assumed that the prostatectomy was done for benign hypertrophy. The state of the kidneys at that time is not mentioned. It is customary to investigate the kidneys before prostatectomy, particularly after an episode of acute retention, but the record does not state whether such examination was made, consequently, one is not justified in assuming that the left kidney and ureter were normal.

DR. BENJAMIN CASTLEMAN No pyelograms were done at the other hospital.

DR. SIMEONE It is natural to ask if the present illness could have been a late sequela or complication of suprapubic prostatectomy. The pyelonephritis and subsequent perinephric abscess could have resulted from chronic obstruction of the urinary tract. Massive hemorrhage is possible but rather infrequent. The process is bilateral and involves the ureters. The x-ray studies done in this hospital do not suggest such involvement.

The most significant fact is the painless hematuria for seven years in a seventy-one-year-old man. It is reasonable to assume that whatever caused the hematuria was responsible for the pyelonephritis and for the extension of the infection into the perinephric tissues. The record states that blood was seen to come from the left ureter. That excludes from the causes of hematuria the numerous associated systemic conditions and limits the possibilities considerably. In addition blood was flowing not only from the ureter but also from the renal pelvis, because it was obtained from the ureteral catheter that was passed 25 cm — well into the renal pelvis. The additional information is that cystoscopy revealed no cause for the bleeding in the bladder. If a papilloma of the bladder had been present at cystoscopy and operation six years previously, and if a small section of the lesion had been removed, there should have been residual evidence of the lesion at examination in this hospital. There was reddening around the ureter, with nubblike projections about the ureteral orifice, a biopsy of which showed malakoplakia. Perhaps Dr. Castleman will tell us more about the histology of this lesion. Attempts have been made to relate malakoplakia to tuberculosis or mycotic infection in the kidney, but the evidence is not generally accepted and about all that one can say about malakoplakia

is that the condition is associated with chronic and prolonged infections in the kidney, ureter and bladder.^{1, 2}

This brings the discussion to the point that is usually reached in trying to determine the cause of hematuria, and help from the roentgenologist is needed. The record states that there was a filling defect in the renal pelvis and neck of the calyx. It might be interesting to have Dr. Schulz show the films.

DR. MILFORD D. SCHULZ: These films, which are representative of the two examinations made, show a definite pressure defect on the calyces, which are rather ragged in outline and larger than usual. The kidney outline is not visible. There is no calcification in the kidneys, merely dye extravasated into the destroyed kidney parenchyma. The ureter is not visible.

DR. SIMEONE: Is there any irregularity in the calyx itself at that point?

DR. SCHULZ: I do not know. Certainly it looks as if something is compressing it. A lateral film would be helpful.

DR. SIMEONE: Can you be certain whether the filling defect is caused by a lesion outside or within the pelvis?

DR. SCHULZ: I think that it is probably outside the pelvis, but whether or not it is outside the kidney I am not sure. It seems as though the pelvis is being pressed on by some mass.

DR. SIMEONE: Is this calyx dilated?

DR. SCHULZ: All are wider than they should be.

DR. SIMEONE: Is there any evidence of nonopaque stone obstructing the ureteropelvic junction?

DR. SCHULZ: None that I can see. This is Paget's disease down here in the pelvis, that is the only part of which I am sure.

DR. SIMEONE: One can explain the trabeculations in the bones of the pelvis, as Dr. Schulz has said, on the basis of Paget's disease. I do not know any way of connecting the bone disease with the renal lesion. In reviewing some of the possible causes of hematuria in this case, the record of brown pus from the abscess and the slight enlargement of the liver suggested amebic abscess, but I do not know of amebic abscesses that occur in the kidney as they do in the liver. The roentgenograms and the characteristics of the aspirated pus are not consistent with actinomycosis or tuberculosis, which could account for both the hematuria and the chronic infection resulting in the malakoplakia. Tuberculosis as a cause of painless hematuria is unusual in a patient of this age. Painless hematuria occurs early in tuberculosis of the kidney, and renal tuberculosis is generally found under the age of forty. I do not believe that there is evidence of stone, opaque or nonopaque.

The diagnosis of tumor and infection therefore remains. The only question remaining is what type of tumor was present. If the hematuria had been due to this tumor and had lasted for seven years,

malignant tumor, although possible, would be unusual. The roentgenogram is consistent with either a malignant tumor or a benign cyst. If the latter had been the lesion involved, it is conceivable that the aspiration of brownish fluid would have come from the cyst rather than from a perinephric abscess. All the findings, however, favor perinephric abscess. My diagnosis is tumor of the kidney, probably a cyst, with perinephric abscess and acute and chronic pyelonephritis.

DR. WYLAND F. LEADBETTER, JR.: We worried for some time about the diagnosis in this case. A fluctuant mass was present in the flank from which we aspirated pus, on the basis of which we believed that the patient had a perinephric abscess. We were unable to ascribe a definite diagnosis to the kidney lesion itself. The main criticism up to this point is that we did not have the necessary x-ray films. We should have had oblique and lateral films, which would probably have given considerable help.

CLINICAL DIAGNOSES

Perinephric abscess, possibly secondary to tumor of kidney

Pyelonephritis, acute and chronic

DR. SIMEONE'S DIAGNOSES

Perinephric abscess, secondary to tumor of the kidney, probably benign cyst

Pyelonephritis, acute and chronic

ANATOMICAL DIAGNOSES

Perinephric abscess secondary to renal-cell carcinoma

Pyelonephritis, acute and chronic

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: At operation the surgeon found an abscess on the posterior aspect of the kidney over Gerota's capsule. A large quantity of purulent material was drained from it. Further exploration of the kidney, however, showed that its posterior aspect, beyond this abscess, contained a great deal of necrotic material, which grossly suggested a tumor. For that reason the entire mass was removed after the incision was extended upward for a considerable distance. The mass, which was removed in two pieces, because it was so necrotic, proved to be an unusual renal-cell carcinoma. It was quite slowly growing, and it is not inconceivable that this neoplasm had been present for seven years. We have had a number of cases in which the tumor was present for a long time.

The patient was seen yesterday afternoon at the Tumor Clinic, and the note by the physician who saw him states that there had been no further hematuria, the patient felt fine, the urine was clear, and nothing could be felt in the flank.

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MATERNAL AND CHILD WELFARE

THE altercation between Senators Taft and Murray during the recent hearings on the Wagner-Murray-Dingell Bill, although an unfortunate reflection on the dignity of the highest legislative body in the land, had the merit of dramatizing an encouraging phenomenon in the midst of discord the need for better medical, hospital and nursing care for all people in the United States is recognized by all parties. Disagreements represent conflicting opinions regarding methods and are not concerned with denying that improvement must be provided, the opponents of the bill objecting to any extension of government paternalism and interference and the supporters claiming that only through legislation can better care for all classes of

citizens be guaranteed. If the latter ideology is not to prevail, the medical profession must accept the responsibility of inaugurating the reform that is unanimously demanded.

A crucial part of any program, compulsory or voluntary, for the extension of medical care is adequate provision for the health and welfare of mothers and children. Numerous flaws in the Government's attempt to remedy the existing shortcomings in this field—the Pepper Bill—have been pointed out.¹ This is not to say that the objectives of the bill, as stated in the introduction, do not have the full approval of the medical profession. But the methods by which those objectives are to be achieved represent not only a threat to many basic ideals and principles of the profession but also, in many respects, an inefficient and unworkable approach that may well work to the disadvantage of the classes that the bill is designed to benefit.

This and similar legislation offers a challenge to the medical profession. If government interference is to be averted, the inadequacies and inequities of maternal and infant care in many areas, particularly among indigent classes, must be recognized and corrected by the concerted effort of physicians. The following factors in the care of all mothers and infants must be given special consideration: the need for obstetricians qualified by training and experience to provide adequate care in pregnancy, labor and delivery, as well as post partum, adequate nursing care and instruction to prepare the new mother for the duties of parenthood, access to special consultation services in the event of complications, hospitals with sufficient staffs and facilities to furnish continuous maternal and infant care, and the benefit of the newest and best developments in diagnosis and therapy, regardless of cost. A notable example of what can be accomplished by a voluntary approach to the problem is provided by the Chicago Lying-in Hospital.² During the past thirteen and a half years 47,945 obstetric patients were cared for at this institution, with 81 deaths, a mortality rate of 0.17 per cent, but during that period the mortality rate fell from 0.42 per cent in 1931 to zero in 1944. Undoubtedly such an outstanding achievement cannot be obtained in

all parts of the country, but it can be and is being approached. The pattern of the Blue Cross and the Blue Shield should be extended to include all sections of the country, all classes of the population and all types of medical care existing programs of prepayment hospital and medical care offer proof that the medical profession can take the lead in co-operation for the public welfare.

Democracy often works in strange and wondrous ways, the existence of inequalities being a major paradox. In many states the Negro is disenfranchised, and efforts to remedy the injustice are met with opposition and terrorization of the subject race, in other parts of the country the necessities of life and health are beyond the reach of a large segment of the population. When such inequalities are discussed in the halls of Congress and, what is more important, constructive attempts at correction are undertaken by the groups most intimately concerned, the fullest benefits of our way of life offer promise of realization. The role of physicians in these efforts is vital.

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DIAGNOSIS OF MALARIA

Two papers appearing elsewhere in this issue of the *Journal* serve as useful examples to point out problems that confront civilian physicians in diagnosing and treating malaria. These are occurring with sufficient frequency to warrant emphasis on methods for their solution. Three primary situations exist. Discharged veterans or men on inactive duty who were exposed to infection in malarious areas while under suppressive treatment are likely to come down with delayed primary attacks of vivax malaria. A previous history of malarial attacks caused by *Plasmodium vivax* is the basis for subsequent relapses over a period of one to three years. Finally, malaria may develop in a patient receiving transfusions of fresh or stored whole blood from donors who are infected with benign tertian or quartan malaria. No figures are available for the actual frequency of each of these situations.

Nevertheless, acquaintance with the underlying facts obtained from the extensive experience of others is pertinent to physicians who are likely to be consulted by persons who served in endemic malarious areas.

The protean character of primary attacks of malaria is well illustrated by London and Most in their warning about differential diagnosis. Bacterial and certain viral infections must be distinguished from malaria. Abdominal symptoms simulating an acute surgical abdomen may also occur during the first few days of clinical malaria. The number, type and intensity of symptoms of primary malarial attacks unfortunately are seldom typical in the textbook sense. Thus, before a diagnosis is made on clinical evidence and treatment is begun, the blood should be thoroughly examined for malarial parasites. The immediate prescription of chemotherapy with sulfonamides or antimalarial drugs without adequate search for parasites only prolongs the time required to make a positive diagnosis and administer curative treatment.

The search for plasmodia before the intervention of chemotherapy frequently fails because of the low incidence of the organisms during the beginning of the primary clinical attack. As few as ten parasites or less per cubic millimeter are sufficient to cause the first febrile attack.¹ According to the figures of London and Most, 54 per cent of the primary attacks and 31 per cent of the relapses with *P. vivax* had less than a thousand parasites per cubic millimeter of blood or approximately one parasite for five thousand erythrocytes. Thus, to request a routine laboratory examination for malarial parasites is not enough. The diagnosis should be made by persons with experience in the improved thick-film and thin-film staining techniques and in the specific identification of the parasites. For low concentrations of parasites, the thick-film methods using the Giemsa, Wright-Giemsa or other suitable staining procedures must be employed for satisfactory results. A routine Wright's stain of the blood films does not ordinarily demonstrate the parasites. Failure to find the parasites is usually detrimental to the patient, since it misleads the clinician in prescribing treatment.

If the patient is carrying malarial parasites and

not properly treated, transmission of the disease to others by anopheline mosquitoes becomes possible. In the northern part of this country, the breeding season for vectors of malaria is limited to the midsummer months. In the midland and southern United States, however, transmission is possible for a greater part of the year. Since Young et al.² have proved that native anophelines, *Anopheles quadrimaculatus* and *A. punctipennis*, can transmit malarias of foreign origin and that patients are infectious for anopheline mosquitoes so long as they are subject to relapse, early diagnosis and effective treatment are desirable for control purposes.

That transfusions with whole blood can lead to clinical malaria has been known in this area for many years.³ In the case cited by Fischer and York transfusion of whole blood stored five to twelve days leads to malaria, and this can be expected to happen more frequently as the methods for preserving whole blood improve. The submicroscopical levels of circulating parasites in these donors with a previous malarial history and the absence of an effective serologic method to detect latent infection leave no alternative other than the rejection of blood from those who have had a past infection, however remote. The relatively long incubation period of transfusion malaria in many cases and the low grade of parasitemia are the features that may confuse the clinician. Here again, blood films should be prepared and examined by skilled technicians to arrive at the correct diagnosis.

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MASSACHUSETTS MEDICAL SOCIETY

DEATH

SULZBACH — Wolfgang Max Ferdinand Sulzbach, M.D. of Boston, died recently. He was in his thirty-eighth year. Dr. Sulzbach received his degree from Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn, Prussia in 1933. He was a member of the staff of the McLean Hospital.

MISCELLANY

PROGRAM ON CARE OF THE HEART

Interest in the control of heart disease is currently being enhanced by the efforts of many professional and lay groups. This attention to heart ailments has long been warranted. The public is becoming more acutely aware of cardiac hygiene than ever before — a growing interest that should be cultivated and guided with judgment as well as vigor.

During the past third of a century, the improvement in mortality from heart disease was most pronounced in the younger age groups and decreased progressively with advance in age. The death rate from diseases of the heart and arteries, corrected for the aging of the population, dropped virtually 30 per cent between 1911-15 and 1940-44, according to experience among the industrial policyholders of the Metropolitan Life Insurance Company. This reduction in mortality from the principal cardiovascular-renal diseases has been particularly marked among white females — 37 per cent in the above-mentioned period. Among males, the decrease in mortality, although not so marked as that among females, was 25 per cent, still a substantial reduction. This still leaves much to be desired in the field of early diagnosis and immediate initiation of adequate cardiac regimes to reduce to a minimum incapacity and mortality from these conditions. Concentration of effort must now be placed on teaching the public what is known about prevention, early recognition and care of cardiac lesions.

To assist in the attainment of this goal, the Metropolitan Life Insurance Company is conducting a special campaign on heart disease during the fall and winter months. At that time, more than 20,000 field representatives, in co-operation with official and voluntary agencies, will reach the homes of millions of policyholders with a recently published pamphlet, "Your Heart," developed in co-operation with the American Heart Association. A lay educational film on heart disease is also being prepared. Distribution will be made to physicians of a packet in which will be included material of special interest to doctors. A scientific exhibit on heart disease, first shown at the meeting of the American Medical Association in San Francisco, is available for state and local professional meetings.

BOOK REVIEWS

Periodontal Diseases and Soft Tissue Lesions of the Oral Cavity: Diagnosis and Treatment. By Arthur H. Merritt, M.S., D.D.S., Sc.D. Third edition. 8°, cloth, 256 pp., with 53 illustrations. New York: Macmillan Company, 1945. \$3.50.

The third edition of this book has an added section, consisting of six short chapters and nine illustrations, entitled "Soft Tissue Lesions of the Oral Cavity." In the opinion of the reviewer, this section, which gives a superficial and inadequate discussion of lesions of the mucous membrane, with a few rather poor illustrations, detracts from rather than enhances the value of the book, which offers useful practical information — based on extensive clinical experience in the diagnosis and treatment of periodontal diseases — regarding the management in office practice.

Recent advances in the knowledge of periodontal diseases are not referred to, and the bibliography is incomplete and fails to satisfy the inquiring mind of the student or practitioner of dentistry.

The Psychology of Women: A psychoanalytic interpretation. Volume II. *Motherhood*. By Helene Deutsch, M.D. 8°, cloth, 498 pp. New York: Grune and Stratton, 1945. \$4.50.

Rarely does a reviewer have the pleasure of studying a book of this type. Dr. Deutsch has presented her second volume of this broad and controversial field with a clarity, construction and determined purposefulness that is often lacking in psychologic and psychoanalytic literature. The reviewer highly recommends this book to all professional members of allied psychiatric services.

The text develops the theme of most of the psychologic, really psychoanalytic, factors in maturing and older women. The chapters that seemed to have outstanding informative clarity were those on pregnancy, confinement and lactation and the mother-child relation.

Some features with which the reviewer personally takes issue are offered. In the first place, there seems to be a tendency to generalize on the subject of social stresses, which, of course, makes the text more popularly interesting, this might also be said concerning the subject of matriarchy versus patriarchy. Secondly, as in other psychoanalytic texts, the ascribing of deeper, unconscious motives for scientific investigations in social and anthropologic fields was noted. Considerable discussion could center about the difference between maternal instinct and motherliness (mother love). Dr Deutsch places emphasis on the latter almost as though it were a separate entity. To the reviewer, motherliness seems to be a more highly developed expression of maternal instinct, with volitions and inhibitions proportionately more highly developed. In this respect the psychologic expression "rich determinants of emotional motherhood" seems to be part of the entire process of adaptation to inner and outer tensions rather than a subject set apart for strictly psychoanalytic study. Another item of issue is that Dr Deutsch, throughout the text, apparently found difficulty in properly evaluating biologic and physiologic elements and sometimes verbally set them aside, only to bring them up repeatedly in connection with processes unexplainable by psychoanalytic methods. Yet considerable space was devoted to the physiology of the sexual act and organic components thereof. Still another point to be clarified is the thesis that pregnancy is often fortuitous and accidental, but that cultural actions, customs and taboos make for compensatory conscious acceptance of the fetus whereas unconscious factors may be varied and changeable, one might also question the emphasis placed on drives toward achieving motherhood.

A fuller discussion of the psychologic factors in pregnancy and motherliness in Fascist cultures, as well as more consideration of the same subject in Egyptian and Greco-Roman civilizations, would have been of greater value than the devoting of so much space to more primitive social levels and literary subjects.

Considerable positive acclaim is given to the "motherly woman," with the implication that this type of woman is the best for adjustment and mature gratifications. The reviewer again states that the book is professionally adequate, quite informative and effortless to read.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Conscience and Society. A study of the psychological prerequisites of law and order. By Ranyard West, M.D. (Lond.), D.Ph. (Oxon.) 8°, cloth, 261 pp. New York: Emerson Books, Incorporated, 1945. \$3.00.

Dr West believes that world-wide law (government and society) must be based on human nature as it is, not as prejudice makes it out to be, and that laws must be psychologically sound. The work is divided into three parts. The first is a study of human nature, including a discussion of three of its philosophies (those of Thomas Hobbes, John Locke and Jean Jacques Rousseau), human government, as viewed through the ages, the psychologic theories of human nature and the actual behavior of man. The second is a study of the control of human nature by law, comprising chapters on a psychologic theory of law and the stage of social organization represented by present international law. The third part attempts to apply present knowledge of man's social nature to present problems of social organization and world order under the headings of the emotion of loyalty and manipulation of world forces to attain world law.

Dr West is a psychoanalyst, and under the headings of psychologic theories of human nature and the actual behavior of man he devotes more than a third of his text to psychoanalysis, in which he discusses the principles of psychoanalysis, the findings of Freud in neurosis, Freud's theory of human nature (with case material) and the psychologic theories of human nature that contrast with that of Freud. The behavior of man is discussed under the headings of instinct in action, observations of child psychology, and psycho-

analytic reactions and real life side by side. This last chapter is extensively documented with case histories. The book should be useful to all persons interested in psychoanalysis.

Report of the National Health Survey. Conducted by Canadian Medical Procurement and Assignment Board. 8°, paper, 336 pp. Ottawa: Edmond Cloutier, 1945.

This extensive detailed report is divided into eight parts: civilian medical manpower, medical schools, public health, hospital personnel and facilities, industrial medicine, medical services, nursing services and dental services. Various governmental orders and statistical tables are included in a large appendix.

The Physiology of the Newborn Infant. By Clement A. Smith, M.D., professor of pediatrics, Wayne University College of Medicine, and medical director, The Children's Hospital of Michigan. 8°, cloth, 312 pp. Springfield, Illinois: Charles C. Thomas, 1945. \$5.50.

In this monograph Dr Smith considers the fetal and neonatal physiology of the child in its various aspects. He divides his subject as follows: respiration, circulatory system, blood (with a chapter on icterus neonatorum), metabolism and heat regulation, the digestive tract, nutrition, kidneys, endocrinology and immunology. The text is well documented, a lengthy list of pertinent references being appended to each chapter. The book is well printed on good paper, with a good type. This monograph should be in all medical reference collections and in the libraries of pediatricians and obstetricians.

Recent Advances in Obstetrics and Gynecology. By Aleck W. Bourne, M.A., M.B., B.Ch. (Camb.), F.R.C.S. (Eng.), F.R.C.O.G., obstetric surgeon, St. Mary's Hospital, consulting obstetric surgeon, Queen Charlotte's Hospital, and consulting surgeon, Samaritan Hospital for Women, and Leslie H. Williams, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.C.O.G., obstetric surgeon to out-patients, St. Mary's Hospital, consulting obstetric surgeon, Queen Charlotte's Hospital, the Jewish Maternity Hospital and the Nelson Hospital, surgeon to in-patients, Samaritan Hospital for Women, and examiner in midwifery and gynecology, University of Cambridge and Conjoint Board. Sixth edition. 12°, cloth, 357 pp., with 77 illustrations. Philadelphia: The Blakiston Company, 1945. \$5.50.

The first edition of this well known review of obstetrics and gynecology was published in 1926. Successive editions have been issued every few years to the present time. The authors were surprised to find that much valuable research had been done during the last four war years. A few entirely new chapters have been added to the present edition, namely, nutrition in pregnancy, vitamin K, stillbirth and neonatal death and erythroblastosis. There is also a new chapter on x-ray therapy in gynecology, which has been separated from the chapter on radiologic diagnosis. Certain chapters appearing in previous editions have been discarded, such as antenatal care, pyelitis, puerperal sepsis and electrophysical therapy. It should be noted that only three chapters remain from the first edition of 1926, all of which have been thoroughly revised and brought up to date. In the light of this fact, all editions of this book should be in every reference collection on obstetrics and gynecology.

NOTICES

ANNOUNCEMENTS

Dr Edward C. Dyer announces the opening of an office for the practice of pediatrics at 330 Dartmouth Street, Boston.

Dr Benjamin I. Nadelman announces his return from military service and the reopening of his office for the general practice of medicine at 140 Blue Hill Avenue, Roxbury.

Dr John A. Reidy announces the removal of his office to 1101 Beacon Street, Brookline, for the practice of orthopedic surgery.

Dr Irving Silverman announces his return from military service and resumption of the practice of pediatrics at 416 Marlborough Street, Boston.

(Notices continued on page xix)

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CLINICAL MALNUTRITION IN ITALY IN 1945*

Nutritional Status of Selected Population Groups

JACK METCOFF, M.D.,† AND ANDREW J. McQUEENEY, M.D.‡

BOSTON, MASSACHUSETTS, AND BETHESDA, MARYLAND

THIS report describes a practical survey procedure for rapid clinical assessment of the nutritional status of selected population groups within a given community or area. It summarizes the results of thirty-five such studies performed in Italy during the winter, spring and summer of 1945. Approximately 4000 persons were examined. Data derived from 3109 children and pregnant or nursing women selected from refugee, institutionalized, school and population-at-large groups are presented.

By rapid, standardized assessment operations, carried out over a wide geographic area and utilizing a consistent weighted sampling technic, it was possible to gather epidemiologic information on malnutrition. This implies the determination of the extent, distribution, type and severity of existent clinical malnutrition, as evidenced by generally accepted diagnostic signs and supported by simple laboratory procedures. Data gathered in this manner were recorded on standardized punch cards, promptly analyzed and reported and used as the basis for recommendations that guided concurrent feeding operations.

GEOGRAPHIC LOCATION AND POPULATION GROUPS

Thirty-five individual nutrition surveys were performed in a wide geographic zone that included a portion of southern Italy, as well as the central and northern regions (Fig. 1).

Detailed studies were made in the Rome, Florence and Milan regions, each area had characteristic ethnic and socioeconomic differences — often accentuated by wartime alterations in transportation, housing and sanitation. Because of migration from the comparatively localized areas of destruction toward relatively intact cities, the main bulk of the population studied was urban, although several semirural and rural groups were investigated. In

each survey attention was directed toward various stress population groups in which circumstances were weighted in favor of malnutrition.

The 4000 Italians examined were composed almost exclusively of children and pregnant or nursing

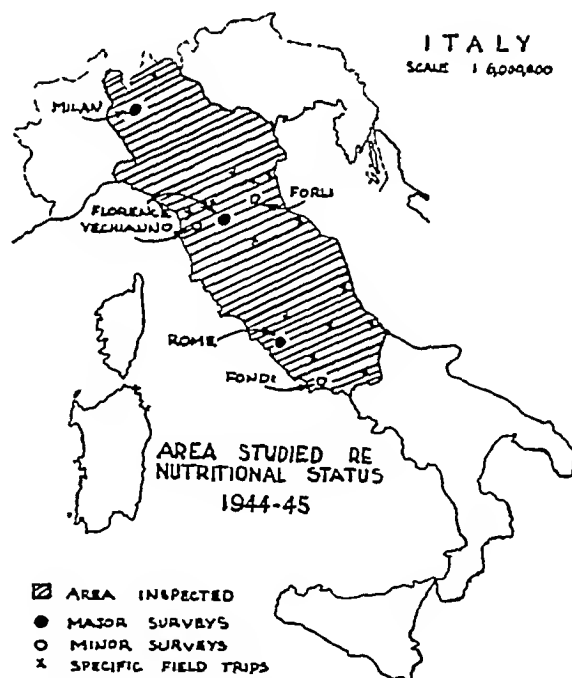


FIGURE 1 Geographic Zones Involved in Nutrition-Survey Studies

The circles represent general areas in which groups of both urban and semirural surveys were centered.

women drawn from schools, from the general population and from institutions. School children were studied in Rome, Florence, Forlì and Milan. In the same areas and in Vichiano, the general population was encountered principally within maternal and child-welfare stations. Refugee groups of dis-

*This study was carried out as part of the integrated activity of the Health Division Italian Mission, United Nations Relief and Rehabilitation Administration. Dr. D. A. Reekie, Senior Surgeon (R) USPHS, director, and the Nutrition Section, European Regional Office, United Nations Relief and Rehabilitation Administration, Dr. A. P. Meiklejohn, senior officer.

†Research fellow, Department of Nutrition, School of Public Health and Department of Biochemistry, School of Medicine, Harvard University.

‡Senior assistant surgeon (R) USPHS, Pathology Division, National Institute of Health, Bethesda, Maryland.

placed Italians were examined in the vicinity of Rome and Forlì. Institutionalized populations were drawn from state and private orphan asylums, foundling homes and penal institutions of the various areas.

METHODS OF SELECTION

The purpose of the sampling procedure employed was to obtain information regarding the nutritional status of a large population group by standardized examination of only a representative sample of the total group. True random sampling of a total population was not feasible, since the required statistics either were not available or had lost their validity, but by deliberately introducing a factor of selection in addition to the factor of chance, it was possible to modify and direct subsequent results in a predetermined and specific direction in such fashion as to disclose existent malnutrition. This, in general, was accomplished in two ways. First, in accordance with the weighted sampling procedure that Meiklejohn¹ developed in his Wales surveys, pregnant or lactating women and children who were experiencing rapid growth spurts were

served to indicate the aim and method of the study and to stimulate the necessary interest and cooperation. Specific routine questioning was designed to achieve subdivision of the area into smaller compartments, each roughly homogeneous from a socioeconomic standpoint. Within each homogeneous zone, foci of nutritional need were further localized among school, refugee or institutionalized populations on the basis of the best available data. The resultant information afforded quite reliable selection of six to eight representative examples of the neediest schools, institutions and clinics in divergent parts of the community.

Data pertaining to further definition of the population to be studied were obtained at each selected school or institution, and nominal lists of actual attendees, grouped by age or class, were inspected. An appropriate sample was attained by arbitrarily selecting from the lists each *N*th individual, *N* being determined in relation to actual attendance per age group. The sample size varied from 13 to 100 per cent of the sample eligibles (Table 1). The name, age, sex and place of origin of the selected subject

TABLE 1 Number of Cases Examined according to Area and Population Group*

AREA	TOTAL ESTIMATED CENSUS	CENSUS DATA			PERCENTAGE OF ELIGIBLES EXAMINED	CASES EXAMINED		
		ACTUAL CENSUS OF SELECTED AREA	SAMPLE ELIGIBLES IN SELECTED AREA†			CHILDREN	PREGNANT OR LACTATING WOMEN	TOTAL
Saote Croce and Cioecitta	4,970	3,000	1,850	13		267	73‡	340
Rome schools	112,000	6,020	4,428	25		1,109	0	1,109
Rome institutions	16,880	981	730	75		372	396‡	768
Florence schools	17,552	320	300	30		125	0	125
Florence institutions	3,751	312	312	36		104	80	184
Forlì schools, institutions and refugees	8,000	1,190						
Vechiann	1,100	1,000	256	67		172	17	189
Milan schools and institutions	110,000	2,124	600	17		89	11	100
Totals	274,253	14,947	1,300	23		295	0	295
			9,776	32		2,533	577	3,110

*More than 1000 cases examined in association with Unitarian Coögregational Medical Nutrition Mission at Foudi and Poitecorvo are not included.

†Eligibility depended on three factors: age groups, pregnancy or lactation and actual attendance at school or institution.

‡Includes 75 to 80 per cent of pregnant or lactating women.

deliberately selected as representing physiologic stress groups likeliest to manifest clinical evidence of malnutrition. These categories were recipients of special allowances, but it seemed unlikely that the minimal dietary supplementation would have significantly altered their status. Secondly, on the basis of carefully evaluated local information from various sources, mothers and children from poorer socioeconomic areas were chosen. It was believed that such selection would provide a heavily weighted sample representative of the worst—rather than the average—nutrition in a given area. From a physiologic standpoint, it seemed probable that if these selected groups showed little evidence of malnutrition, no significant amount of malnutrition would exist in the remaining population.

In practice, the first contacts in any urban area were with a responsible Italian official and often with the local health officer. A short conference

were inscribed by local personnel on standard punch cards. Each child or mother was then prepared for examination and queued at an appointed hour with the punch card in hand.

This general procedure was duplicated in dealing with semi-official and private organizations. In some, particularly in several refugee camps and in the general-population studies in rural or semirural areas, the procedure varied slightly. Family or dwelling units were used as the basis for area sampling within the confines of a given camp, and a total census of pregnant and nursing mothers attending maternal and child health centers in rural or semirural areas was frequently examined. In general, careful sample selection and local preparations for examination of subjects from any one area rarely required more than twenty-four to forty-eight hours, and the examination itself, rarely more than two to four hours.

EXAMINATION PROCEDURE AND REPORTING

CLINICAL CRITERIA

The basic examination procedure consisted of a rapid inspection for signs of deficiency disease: the condition of the skin of the hands, arms, legs and thorax was noted, and the eyes, nose, lips, teeth, gums, tongue, ears, neck and skeletal structures were examined. Neurologic examination was limited to observation of gait, calf and nerve tenderness in the lower extremities, when these signs were positive, reflexes and vibration sense were tested. The presence of visible, palpable thyroid enlargement and of edema was noted. Data on height and weight were collected routinely. In most cases, Sahli hemoglobin determinations, by means of earlobe punctures, were carried out on alternate subjects in the sample concerned.

It was planned to perform gravimetric copper-sulfate protein determinations² in the field, with the exception of rare cases of infantile inanition encountered in pediatric hospitals or foundling homes, however, no subjects were observed in whom plasma-protein determinations seemed clinically indicated. Consequently, protein determinations were carried out only in the rare event that pediatric hospital laboratory facilities were functioning and accessible. No satisfactory field apparatus for measuring plasma volume was available. There is laboratory evidence that determination of plasma-protein concentration, without concomitant plasma-volume measurement, yields misleading and equivocal data, particularly in protein deficiency states.^{3, 4}

Except for infants, patients were only partially disrobed. The thorax and abdomen of mothers were not examined routinely. Two physicians alternated in the performance of clinical examinations and Sahli hemoglobin determinations. A relatively high degree of similarity in technic and diagnosis was attained by both observers. Diagnoses were recorded by means of a moderately complete, systematized numerical code that involved approximately one hundred and twenty clinical signs of deficiency disease, the numbers of which had been printed on the standard survey cards.⁵ After short experience, code numbers of the majority of signs were easily recalled. During the course of the examination, numbers on a given patient's card corresponding to observed signs were circled by an assistant. This method of recording observations was found to be quite efficient in minimizing friction, error and delay. Recording of hemoglobin levels in terms of fairly broad ranges contributed to ease in performance and subsequent analysis.

On completion of a survey, the card of each subject was punched in accordance with the numbers circled on it. All cards were sorted, and the data transcribed on detailed standard work sheets, analyzed and reported, usually within twenty-four to forty-eight hours after completion of the survey.

Since various biochemical lesions of mild deficiency states cannot be readily and conclusively detected at a clinical level without associated laboratory aids,⁶ the categorization of malnutrition was restricted to classic deficiency disease. There are considerable variations in the criteria used for such diagnoses, but in these studies the following were required.

Rickets All subjects had at least three skeletal signs of rickets, including marked frontoparietal bossing with or without craniotabes, Harrison's groove, marked enlargement of costochondral junctions (so-called "beading" or "rosary"), clinically enlarged epiphyses or deformity of the long bones — the last being defined as deformity of lower extremities of such a degree that the distance between malleoli at proximal or distal ends of the tibiae was 3 cm or more. No roentgenographic or laboratory facilities for corroborative diagnosis or for determination and assessment of rachitic activity were available. Consequently all rickets in children four years of age or over was diagnosed as inactive or old, rickets in younger children was arbitrarily called active or recent on the basis of physiologic and statistical chance.^{7, 8}

Ariboflavinosis All cases so diagnosed had cheilosis, that is, angular stomatitis associated with denudation with or without fissuring of the lower lip, magenta tongue with fungiform hypertrophy and sometimes classic nasomalar seborrheic dermatosis. Circumlimbal injection was noted but was not considered in the diagnosis.

Vitamin A deficiency All cases so categorized were observed in subjects with lackluster dryness of the conjunctivas and moderate or marked conjunctival thickening (excluding pterygia and pingueculas), with or without Bitot's spots, as well as typical keratosis follicularis of both upper and lower extremities. Acneform and impetiginous skin lesions were noted but were not requisite for the diagnosis.

Inanition In all such cases there were obvious loss of subcutaneous tissue, dehydration, loss of turgor with looseness and wrinkling of the skin, prominent bones and protuberant abdomen, with associated growth retardation or weight loss. The inclusive term "inanition" as applied, therefore, is synonymous with marasmus, infantile dystrophy, infantile atrophy and so forth.

Anemia This diagnosis was arbitrarily designated when Sahli hemoglobin levels of 8 gm per 100 cc. or less in infants under two years of age and 10 gm per 100 cc. or less in children and in adults were observed — normal hemoglobin values for infants under two years of age are approximately 1 or 2 gm less than those for older children and adults.⁹⁻¹¹ These arbitrary levels probably repre-

sented moderately severe anemia, although the range of normal variation is apparently large⁹⁻¹². The standard for the instrument used was 14.6 to 15.6 gm per 100 cc.

Other diseases No lesions typical or strongly suggesting pellagra, beriberi, scurvy or hypoproteinemia were observed*. Associated or conditioning diseases were recorded when evident or when adequate data were available.

RESULTS

Rickets was the most frequent classic deficiency disease observed. The incidence in particular surveys varied from 25 to 30 per cent among school children to 60 per cent among younger children and institutionalized infants. The overall incidence of rickets in the total sample was 27.7 per cent and proportionally equal in the groups over and under four years of age. This overall incidence is somewhat lower than that observed by Follis, Jackson, Eliot and Park¹³ among children of Italian descent in their hospital-population study, although such a comparison is not entirely valid, since the method of diagnosis differed.

Although suggestive signs of ariboflavinosis were often noted among children three to twelve years of age, diagnostic clinical cases were rarely encountered, the incidence varying by surveys from 0 to 2 per cent.

Suggestive signs of vitamin A deficiency were noted occasionally, the incidence of keratosis follicularis, for example, varied by areas from 0 to 22 per cent. No keratomalacia was observed, although the regional occurrence of eye diseases ascribed by Italian physicians to vitamin A deficiency was apparently not infrequent in the prewar years^{14, 15}. The general incidence of clinical vitamin A deficiency approximated 1.5 per cent.

Inanition, noted only among refugee or institutionalized infants two years of age and under, was frequently conditioned by a previous or current infectious process, and was often independent of available food supply. Approximately 3.0 to 7.0 per cent of institutionalized infants were classified as showing inanition — an incidence of 0.7 per cent in the total child population studied. Among the same groups of infants two years of age and under and in some groups of institutionalized preschool children, height and weight values were not infrequently below those for the national average, this might have been anticipated in view of the weighted sampling procedure employed. Neither inanition nor significant degrees of growth retardation were demonstrable among other groups of children studied.

With the exception of the previously mentioned data on institutionalized infants and young children, the 80 percentile range and median values for height

and weight of central and northern Italian preschool and school-age children showed no marked deviations from prewar Italian standards¹⁶.

The incidence of moderately severe anemia varied from 3.0 to 20.0 per cent among institutionalized infants and preschool children, but was only 0.3 per cent among school children and 1.5 per cent among pregnant and lactating women. Since procedures other than hemoglobin determinations were not attempted under existing field conditions, it is quite possible that some of the cases of anemia observed were of non-nutritional origin.

Simple diffuse thyroid enlargement was noted in 5 to 9 per cent of children and in 18 to 23 per cent of pregnant and nursing women. In some samples the incidence of such enlargement in children under ten years of age approached 9 or 10 per cent. The geographic distribution of this finding was fairly uniform. No cases of hyperthyroidism or hypothyroidism and no cretins were seen. The association between thyroid enlargement and fluorosis was not investigated but was observed particularly in Campagna da Roma, where endemic dental fluorosis is almost universal among the static population.

Completely negative examinations were rare (2.0 to 4.5 per cent), and many isolated signs but no other classic deficiency diseases were observed. Gross psychologic or psychomotor alterations, such as apathy, listlessness, excessive irritability, anxiety and depression, were not particularly apparent.

Data pertaining to the incidence of deficiency signs and diagnoses are recorded in Tables 2, 3, 4, 5 and 6.

With the exception of inanition and infantile anemia there was little significant difference in the occurrence of classic deficiency disease in the various population categories of the respective age and sex groups.

DISCUSSION

In thirty-five surveys involving widely scattered stress population groups totaling approximately 4000 subjects, it was not possible to demonstrate any gross clinical malnutrition serious enough in degree or wide enough in distribution to constitute an acute relief feeding problem. With rare exceptions, no deficiencies were encountered that could not have been prevented or successfully treated with cod-liver oil or dry skimmed milk, as well as timely and intelligent pediatric care.

In all surveys such deficiency disease as was encountered consistently followed a fairly uniform pattern indicative of mild chronic or subacute malnutrition. Minor regional differences in the severity of lesions were noted, but the basic pattern of deficiency showed relatively little variation. The mildness and uniformity of the nutritional deficiencies are not particularly surprising when general approximate food consumption, based on budgetary-analysis data gathered by competent workers (Table 7) is considered¹⁷⁻¹⁹.

*Gingivitis was not considered to be of scorbutic origin unless edema, cyanosis, retraction, loss of interdental papillae and bleeding were associated findings. Nonspecific glossitis was noted and described but was not interpreted in relation to any specific deficiency.

TABLE 2 Incidence of Deficiency Disease among 577 Pregnant or Lactating Women according to Population Group

Group	No of Women Examined	NEGATIVE PHYSICAL EXAMINATION			SUGGESTIVE PHYSICAL SIGNS OF DEFICIENCY*			CLASSIC DEFICIENCY DISEASE			Osteo Rickets			ARIDOLAVINOSIS			VITAMIN A DEFICIENCY			ANEMIA†			HEMOGLOBIN DETERMINATIONS [LAPFORMID]		
		NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE	NO OF CASES	PER CENTAGE	PER CASE
Refugees	82	0	0	0	63	76.8	19	23.1	0	0	0	0	4	4.9	0	0	15	18.3	0	0	0	0	0	0	0
Institutional	107	2	1.8	106	97.3	1	0.9	0	0	0	0	0	0	0	0	0	0	0	0	1	1.4	70	64.2	0	
General population	386	8	2.0	378	98.0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	4.3	188	49.0	0	
Totals	577	10	1.7	547	94.8	20	3.5	1	0.2	4	0.7	15	2.6	4	0.7	0	0	4	5.7	4	5.7	238	44.7	0	
Averages																									

*Although such signs were observed, no classic deficiency disease was present
†Diagnosis based on S-hill hemoglobin values of 10 gm per 100 cc or below
Determinations made in 70 cases of total population studied

TABLE 3 Incidence of Deficiency Disease among 2533 Children according to Age and Population Group

Group and Age of Children	No of Children Examined	Negative Physical Examination			Suggestive Physical Signs of Deficiency*			Classic Deficiency Disease			Recent Rickets			Old Rickets			Ariboflavinosis			Vitamin A Deficiency			Inanition			Anemia†			Hemoglobin Determinations Performed		
		No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case	No of Cases	Per Centage	Per Case			
Refugee	71	10	14.0	37	52.1	24	33.8	22	30.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
2 years and under	71	1	1.4	24	33.8	46	64.8	24	33.8	15	21.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
3-5 years	90	0	0	53	58.9	37	41.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
6-9 years	90	0	0	53	58.9	37	41.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
10-15 years	90	2	2.2	56	62.2	32	35.5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0			
Institutional	183	15	8.1	92	50.3	76	41.6	63	34.9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
2 years and under	95	0	0	18	18.9	77	81.0	37	38.9	40	42.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
3-5 years	151	0	0	128	84.8	23	15.2	0	0	22	14.6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
10-15 years																															
General population	63	1	1.9	27	42.8	35	52.4	35	52.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
2 years and under	278	10	3.6	165	59.3	103	37.1	27	9.7	74	26.6	1	0.3	1	0.3	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
3-5 years	829	40	4.8	573	69.1	216	26.0	0	0	227	27.4	11	1.3	3	0.4	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
6-9 years	612	35	5.7	460	75.2	117	19.1	0	0	80	13.1	15	2.4	7	1.1	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
10-15 years																															
Totals	2533	114	4.5	1633	786	31.0	208	8.3	492	19.4	27	1.1	70	2.8	17	0.7	15	1.6	942	37.2											
Averages																															

*Although such signs were observed, no classic deficiency disease was present.

†Diagnosis based on S-hill hemoglobin values of 8 gm per 100 cc or less in infants under two years of age, and values of 10 gm per 100 cc in children over two years of age
Determinations made in 140 institutionalized children under two years of age, in 141 institutionalized children three to five years of age and in 377 children in the general population six to nine years of age

TABLE 6 Deficiency Signs Observed among 2169 Children and Pregnant or Lactating Women in General Population

Group	No. of Subjects Examined	Negative Physical Examination	Proximal Bone	Harrison's Groove	Rachitic Rosary	Bow Legs and Deformity of Lower Bones	Enlarged Epiphysis	Rachitic Pot Belly	Nonspecific Glossitis	Nonspecific Gingivitis	Deformed Lower Lip	Angular Stomatitis	Cretinism	Keratosis Follicularis	Schroeder's Dermatitis	Moderate Conjunctival Thickening	Conjunctival Dryness	Macular Tongue with Follicular Hyperkeratosis	Bitot's Spots	Calc. Trenches	Nasal Trenches	Thyroid Hyperkeratosis
Children																						
2 years of age and under	63	1	47	40	46	5	17	1	17	0	6	6	1	0	6	0	0	0	0	0	0	0
3-5 years of age	278	10	151	130	87	58	107	18	146	6	105	47	23	33	24	9	6	7	0	1	0	22
6-9 years of age	862	42	369	398	243	117	259	0	448	53	432	175	115	116	74	64	3	18	2	5	0	56
10-15 years of age	579	33	184	155	155	54	134	0	511	42	244	103	168	105	77	87	1	19	3	7	0	64
Totals	1782	86	751	723	531	234	517	19	922	101	790	331	207	254	181	160	10	44	5	13	0	142
Percentages		4.8	42.1	40.6	29.8	13.1	29.0	1.1	51.7	5.7	44.3	18.6	11.6	14.3	10.2	9.0	0.6	2.5	0.3	0.7	0	8.0
Pregnant or lactating women	386	8	71	0	0	22	5	0	317	170	110	48	32	11	31	128	5	2	21	27	9	70
Percentages		2.1	18.4	0	0	5.7	1.3	0	82.1	44.0	28.5	12.4	8.3	2.8	8.0	33.6	1.3	0.5	5.5	7.0	2.3	18.3

TABLE 7 Estimate of Average Daily Italian Diet, 1930-1944 *

Group	MILAN (1930) ¹⁷			MILAN (1936) ¹⁸			CUNEO (1944) ¹⁹		
	TOTAL CALORIES	PROT.	FATS	TOTAL CALORIES	PROT.	FATS	TOTAL CALORIES	PROT.	FATS
Urban population	2905	95	89	3003	93	95	2200	78	47
Rural population	3153	94	73	3272	94	73	2700	94	54
Averages	3025	95	81	3135	94	84	2550	86	51

*Data based on studies and analyses of weekly food consumption carried out by trained and experienced workers

The principal Italian dietary alterations associated with war appear to be reduction in dietary fat and carbohydrate, with relative caloric diminution in recent diets. The popularly reported caloric inadequacy of the 1944-1945 Italian ration (900 to 1400 calories) should be interpreted with the realization that approximately only 12 per cent of a person's usual food consumption was derived from ration-card sources, and only about 5 per cent of the weekly food expenditure was utilized for the

of fertilizer, land mining and political flux on present and future crop production is unpredictable, and the accurate assessment of national food reserves is exceedingly difficult.

The high incidence of clinical rickets—277 per cent—is of some interest. Cod-liver oil and concentrated vitamin D preparations were either in short supply or used for therapeutics rather than prophylaxis. Children were often placed in the vicinity of the sun rather than in direct exposure

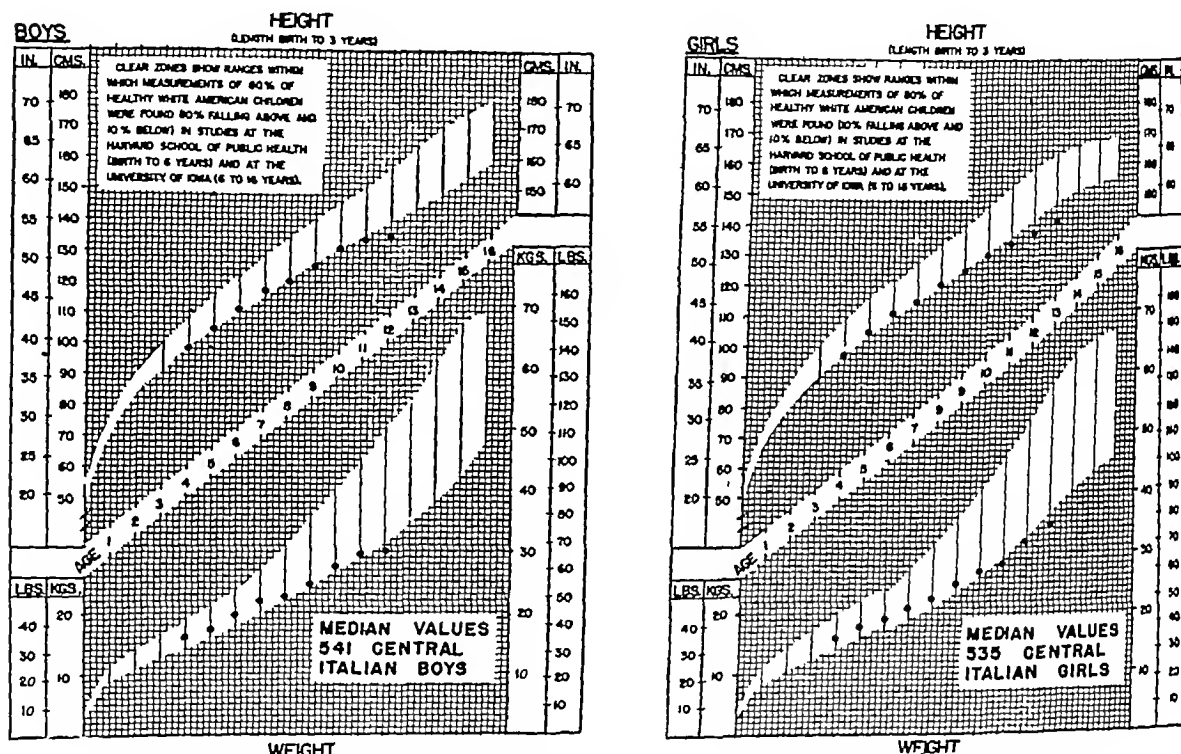


FIGURE 2 Median Values for Heights and Weights of Central (Rome Area) Italian Children of School and Population-at-Large Groups

The values (black dots) are superimposed on charts indicating the 80 percentile ranges for height and weight of normal American children derived from the data of Vickers and Stuart.²⁴ Heights were measured in bare or stockinged feet, and weights in light underclothing, ages were taken to the nearest birthday. Data applicable to 231 institutionalized children in the Rome area were not included. Of these, the medians and 80 percentile ranges of 61 males of four, five and six years of age and 36 females of four and five years of age were consistently lower than the medians charted.

purchase of rationed food.¹⁹ Seventy-five to 90 per cent of the weekly food expenditure was used for purchase of free or black-market foods. In most areas communal restaurants provided calorically adequate, low-cost meals for families in the lower economic bracket. In Milan, for example, approximately two thousand restaurants provided 600,000 persons with daily meals at a usual rate of 4 to 50 lire per meal. Food was usually available, but there is little doubt that the inflationary economy imposed a severe economic burden on fixed-income groups. The effect of such factors as drought, lack

to its rays—a practice that apparently originated from the experience that direct exposure of infants to the spring or summer sun occasionally induced "convulsions and death." In addition, it is quite possible that dietary calcium intake was inadequate, since the relatively low milk and dairy-product consumption^{17, 20} had been further reduced by war. Irrespective of these conditioning factors, the existence and maintenance of numerous hospitals for the treatment of rachitic deformities in children suggest that for generations clinical rickets has been widespread in

school, and population-at-large groups suggests that gross malnutrition was infrequent, that rickets was the only nutritional problem of public-health importance, that there was no conclusive evidence — on the basis of observed deficiencies or growth retardation — that wartime food shortage constituted a major health problem, and that the reported data could probably be duplicated in many areas of the

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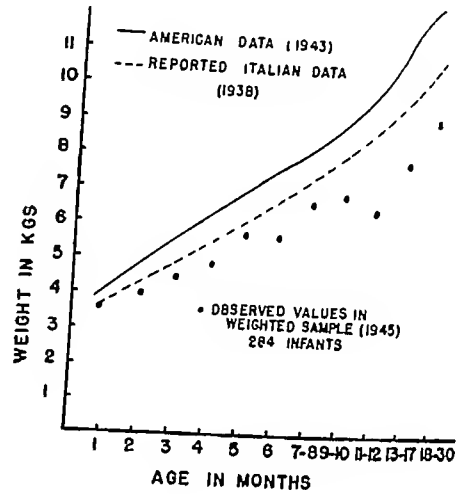
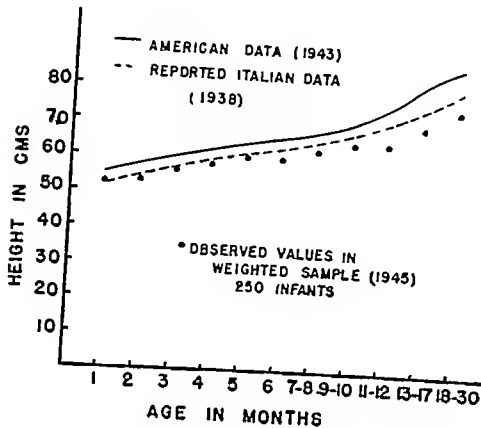


FIGURE 4 Heights and Weights of Italian Infants Compared with Prewar Italian and American Standards. Infants were examined and measured nude. The height represents recumbent length. Because of the weighted sampling technique employed in all surveys, the height-weight values fall consistently below mean prewar values. The trends of both curves are essentially the same. If samples had been weighted in the opposite direction, height-weight values obtained would be expected to fall at approximately the 80 percentile level of a normal distribution curve.

United States if the same method of sampling were employed.

We are indebted to Dr R E Butler, Senior Surgeon, USPHS, and to Dr A P Meiklejohn for their active interest and field sponsorship of this investigation. The technical assistance of Miss Amalia Baran was invaluable, as was the kind co-operation of many Italian physicians, nurses and government officials. Figures 2 and 3 were devised and furnished by Dr Harold Stuart, of the Harvard School of Public Health.

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NONTRAUMATIC SPONTANEOUS PNEUMOTHORAX AMONG MILITARY PERSONNEL*

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THIS study was undertaken with the main purpose of determining the etiologic background and the precipitating factors in cases of nontraumatic spontaneous pneumothorax among hospitalized military personnel. Records covering a ten-year period were reviewed. In the six-year interval from January, 1935, to December, 1940, inclusive, when the military strength of the post was relatively low, there were no cases of spontaneous pneumothorax. In the succeeding four years (January, 1941, to December, 1944, inclusive) 41 cases were encountered. The pertinent military, clinical and roentgenologic aspects are presented and discussed.

MILITARY DATA

The incidence of spontaneous pneumothorax for the years 1942 through 1944, based on the annual hospital admissions of military personnel, was practically constant 0.027 to 0.03 per cent (Table 1). These figures are not valid for comparison

TABLE 1 Incidence of Spontaneous Pneumothorax among Military Personnel

YEAR	NO OF HOSPITAL ADMISSIONS	CASES OF SPONTANEOUS PNEUMOTHORAX	
		NO	PERCENTAGE
1941	48,527	1	0.002
1942	52,947	16	0.03
1943	51,339	14	0.027
1944	52,765	10	0.027

with statistics from civilian institutions, since many soldiers were admitted for conditions that would not necessitate hospitalization in civil life.

The onset of the pneumothorax ranged from four days to eighteen years after entrance into the Army, and the average length of hospitalization was forty-one days. Twenty-nine soldiers were returned to full duty and 4 to limited duty—a total of 80 per cent. Three patients were transferred to a general hospital, 2 because of failure of the lung to re-expand and 1 (an officer) because of recurrent spontaneous pneumothorax. One enlisted man was separated from the service because of a history of multiple episodes of spontaneous collapse of the lung. Two soldiers were discharged because of an associated psychoneurosis. There were 2 patients with far advanced pulmonary tuberculosis, one of whom died, and the other was transferred to a Veterans Administration hospital.

*From the Medical Service Regional Hospital, Fort Bragg, North Carolina.

CLINICAL FEATURES

The remainder of this report is based on 39 patients in whom sufficient clinical and roentgenologic data were available for study (Table 2). All were men, and the average age was twenty-four years and ten months. Four soldiers, or 10 per cent, gave a history of an antecedent spontaneous pneumothorax, in only 1 did the recurrence develop in the military service.

Symptoms

It is logical to assume that the intensity of the initial pulmonary symptoms depends on the size of the rupture, the presence or absence of adhesions or fluid, or both, and the type of pneumothorax—whether closed, open or valvular. The onset was sudden in all but 1 case. Shortness of breath, which was a complaint of all patients, was objectively present in comparatively few. Chest pain, of varying severity, occurred in every patient, and the pain was most frequently localized over the affected lung but sometimes radiated to the shoulder, neck, lower back or abdomen. Cough was present in 7 soldiers, cyanosis in 3, mild collapse in 3, and fever in 2 (active pulmonary tuberculosis).

The relation between physical exertion and the production of a spontaneous pneumothorax is not only of medical interest but also of practical importance from a military viewpoint. The following circumstances at the time of onset were studied (in 1 case an adequate history was not available).

At ease or at rest. It is significant that, in 23 cases (59 per cent), the episode could not be associated with any provoking cause.

Physical effort not specifically related to military activity. Ten soldiers, or 26 per cent, were classified in this group. The exertion was mild (walking).

Physical effort directly related to military activity. Five soldiers, or 13 per cent, gave a history of such exertion immediately prior to collapse of the lung. The military duties performed at the time were as follows: hauling sand, kitchen police, with lifting of heavy utensils, shoveling dirt, running over the obstacle course, and drilling troops.

Physical Signs

The classic signs of air in the pleural cavity are well known. Their prominence depends on the extent of pulmonary collapse and of mobility of the mediastinum. The most constant single sign recorded was diminished or absent breath sounds over the pneumothorax pocket. In all cases, the spontaneous pneumothorax was unilateral. The

lungs were almost equally affected the right in 54 and the left in 46 per cent. None of the patients showed subcutaneous or mediastinal emphysema.

Tuberculin Test

This simple and valuable test was performed in only 12 cases (excluding the 2 patients with active tuberculosis). A positive reaction does not necessarily indicate clinical tuberculosis, but a

these presented no pulmonary lesion on the x-ray film, 2 showed calcified, first-infection-type tuberculosis, and 1, a calcified primary complex with slight linear productive apical infiltration.

ROENTGENOLOGIC FEATURES

Roentgenography of the chest is the most reliable method of diagnosis of pneumothorax. A

TABLE 2 *Clinical and Roentgenologic Data in 41 Cases of Nontraumatic Pneumothorax*

CASE No	AGE	LENGTH OF SERVICE	HOSPITAL STAY	HISTORY OF PHYSICAL EXERTION	CHYAT PAIN	CLINICAL DATA		SIDE AFFECTED	TUBERCULIN TEST	ROENTGENOLOGIC DATA			
						OBJECTIVE DYSPNEA	OTHER SYMPTOMS			PULMONARY LESION	DEGREE OF COLLAPSE†	FLUID	ABST. NOSE
1941	yr	mo	days										
1*	22	9	8										
1942													
2†	21	26	67										
3	25	1	30	None	Mild	None	None	Right	Not performed	None	+	None	None
4	25	9	54	None	Mild	None	None	Right	Not performed	None (incomplete re-expansion)	+	None	None
5	24	17	36	Severe	Mild	None	None	Left	Not performed	None	+	None	None
6	27	10	29	Severe	Mild	None	None	Left	Not performed	None (incomplete re-expansion)	++	Slight	None
7	25	3	52	None	Marked	Moderate	None	Right	Positive	Calcified primary complex	+++	None	None
8	37	216	29	None	Mild	None	None	Right	Not performed	None	+	None	None
9	23	5	11	None	Mild	None	Cough	Right	Not performed	None	+	Slight	None
10	28	7	30	None	Mild	None	Cough	Left	Not performed	None	+	None	None
11	25	13	35	Mild, not related to military duty	Mild	None	None	Left	Not performed	None	++	Slight	None
12	22	1	31	None	Moderate	Moderate	Cyanosis	Left	Not performed	None	+++	None	None
13	29	7	46	None	Marked	Marked	Cough fever and physical collapse	Left	Not performed	Bilateral active tuberculosis	++	Small	None
14	29	3	42	Severe	Moderate	Mild	None	Left	Positive	Calcified primary complex and right fibrotic infiltrate	+	None	None
15	24	9	23	None	Mild	None	None	Right	Not performed	Calcified lymph node on right	+	None	None
16	27	26	42	None	Mild	None	None	Left	Not performed	None	+++	Slight	None
17	25	1	87	Mild not related to military duty	Moderate	Moderate	Cyanosis and collapse	Left	Not performed	Calcified lymph node on right	+++	Slight	None
1943													
18	28	7	40	None	Moderate	Mild	Collapse	Right	Not performed	None	++	Slight	None
19	28	4	20	None	Moderate	Mild	Cyanosis	Right	Not performed	None	+++	None	None
20	20	1	43	Mild not related to military duty	Mild	None	None	Right	Not performed	None	+	None	None
21	24	18	11	Mild not related to military duty	Mild	None	Cough	Right	Negative	None	+	Slight	None

negative test virtually excludes this diagnosis, provided that there are none of the conditions that would depress the allergic response. Six of the 12 soldiers were positive reactors. Three of

film taken at the end of forced expiration is especially valuable in detecting a small collection of air in the pleural space. The findings (Table 2) can be summarized as follows:

Pulmonary Disease

Active, far advanced pulmonary tuberculosis (positive sputum) was found in 2 patients (5 per cent), 1 of whom had a right-sided acute bronchopneumonic process on admission and subsequently developed a spontaneous pneumothorax, with a persistent bronchopleural fistula. The lung showed

right side, and ten days before death a spontaneous collapse developed on the left. The left lung, at autopsy, presented miliary and conglomerate tubercles, caseous foci of varying size, multiple cavities and, in addition, several small, thin-walled emphysematous blebs at the apex. It was the opinion of the pathologist that the spontaneous pneumothorax was due to the rupture of an emphy-

TABLE 2 *Clinical and Roentgenologic Data in 41 Cases of Nontraumatic Pneumothorax (Continued)*

Case No	Age	Length of Service	Hospital Stay	Clinical Data				Roentgenologic Data					
				History of Physical Exertion	Chest Pain	Objective Dyspnea	Other Symptoms	Side Affected	Tuberculin Test	Pulmonary Lesion	Degree of Collapse†	Fluid	Adhesions
1941	yr	mo	days										
22	30	1	26	None	Mild	None	None	Left	Not performed	None	+	None	None
23	19	4	17	None	Mild	None	Cough	Right	Not performed	None	+	None	None
24	21	10	95	None	Mild	None	None	Right	Not performed	None	+	None	None
25	33	1	74	Mild not related to military duty	Mild	Mild	None	Right	Not performed	None	++	None	None
26	25	1	29	Mild not related to military duty	Mild	Mild	None	Right	Not performed	Fibrotic infiltrate at right apex	+	None	Some
27	19	3	29	Severe	Mild	None	None	Right	Not performed	None	++	None	None
28	28	4	24	None	Mild	None	None	Left	Negative	None	+	None	None
29	22	12	7	None	Mild	None	None	Left	Not performed	None	+	None	None
30	30	22	116	No data available	Mild	Mild	None	Left	Not performed	None	++	None	None
31	22	4	27	Severe	Mild	Mild	None	Left	Not performed	None	++	Slight	None
1944													
32	22	39	41	None	Moderate	Mild	None	Right	Positive	None	+	None	None
33	18	1	98	None	Marked	Marked	Cough and fever	Right	Not performed	Acute tuberculous bronchopneumonia on right	+++	Slight	Some
34	22	54	35	None	Mild	Mild	None	Left	Not performed	None	+++	None	None
35	37	23	66	Mild, not related to military duty	Mild	None	None	Right	Positive	Calcified focus on right	+	Slight	None
36	22	21	11	None	Mild	None	None	Right	Positive	None	+	Slight	None
37	23	27	23	None	Mild	None	None	Left	Negative	None	+	Slight	None
38	26	36	46	Mild not related to military duty	Mild	None	None	Left	Positive	None	++	Slight	None
39	20	20	35	Mild not related to military duty	Moderate	Moderate	Cough	Right	Negative	None	++	None	Some
40	19	6	30	Mild not related to military duty	Mild	None	None	Left	Negative	None	+++	None	Some
41	35	28	52	None	Moderate	Mild	None	Right	Not performed	Calcified lymph node on left and fibrotic infiltrate on right	+	None	Some

*Adequate clinical and roentgenologic data not available.

†The degrees of collapse are as follows: +, 5 to 25 per cent; ++, 25 to 45 per cent; and +++, 50 per cent or more.

only slight re-expansion three months later, when the patient was transferred to a Veterans Administration hospital. The second soldier had bilateral tuberculosis, with cavitation and bronchogenic spread. Artificial pneumothorax was induced on the

sematous bleb (one bleb was found open), rather than to a perforating tuberculous lesion.

Inactive, minimal pulmonary tuberculosis (negative sputum) was present in 3 cases, or 8 per cent. In all, the roentgenogram showed unilateral apical

linear productive infiltration. The films also revealed a calcified primary complex in 2 cases, in 1 of which the spontaneous collapse was on the side opposite the reinfection infiltrate. These were the pulmonary findings on admission, and nothing new was noted after re-expansion of the involved lung.

Calcified, primary infection-type tuberculosis only was observed in 4 cases (10 per cent), in 3 of which the pneumothorax occurred on the same side. Again, re-expansion showed no other foci.

No pulmonary process could be demonstrated in 30 cases, or 77 per cent. In 28 cases there was no evidence of pulmonary disease or of emphysematous blebs or bullae after total re-expansion, 2 soldiers were transferred to a general hospital after observation for twenty-seven days in 1 and fifty-four days in the other had failed to reveal significant pulmonary re-expansion, although the visualized lungs were clear.

Extent of Pulmonary Collapse

In the initial roentgenogram taken at the end of inspiration the collapse was considered mild (5 to 25 per cent) in 51 per cent, moderate (30 to 45 per cent) in 26 per cent and marked (50 per cent or more) in 23 per cent of the cases, in the last group x-ray films after re-expansion were negative in 6 cases, 2 showed a healed primary lesion, and 1 revealed active tuberculosis.

Pleural-Fluid Formation

No fluid was observed in 65 per cent, a tiny amount covering the costophrenic angle in 25 per cent, and a small effusion up to the tenth posterior rib in 10 per cent of cases. The 2 soldiers with active tuberculosis, as well as 2 with a calcified first infection, were in this last category. The fluid completely resorbed in all but the 2 soldiers with active tuberculosis.

Adhesions

Adhesions were noted in 13 per cent of cases. Two patients presented no pulmonary lesion after re-expansion, 1 had active tuberculosis, and the remaining 2 had inactive minimal tuberculosis.

TREATMENT

All patients received bed rest, partial or complete. Symptomatic medication to allay apprehensiveness and cough was administered to some. Aspiration of air from the pleural cavity to relieve dyspnea was performed in 3 soldiers, 2 of whom had active pulmonary tuberculosis, these 2 patients were the only ones who also needed oxygen.

DISCUSSION

The problem presented by nontraumatic spontaneous pneumothorax in the Army is not an insignificant one. The important features to be

evaluated are etiology, therapy and military disposition.

Etiology

The immediate cause of spontaneous pneumothorax is a tear of the visceral pleura and the subjacent lung. Many pathologic conditions, however, are responsible for nontraumatic pulmonary collapse. To enumerate them would be superfluous. The chief diagnostic problem is the determination of the presence or absence of tuberculosis as the etiologic agent. It is the consensus that, of the various pulmonary afflictions, tuberculosis is the most frequent. On the basis of autopsy reports, about 10 per cent of patients develop this complication in the course of the disease.¹ The highest incidence is in the actively progressing lesions in which a subpleural cavity or caseous focus, which is free of overlying adhesions, erodes into the pleural cavity. The tearing of adhesions at the base of a necrotic lesion also initiates spontaneous pneumothorax. Furthermore, subpleural emphysematous blebs with rupture may develop, especially in conjunction with fibrotic tuberculous lesions. Their co-existence in a given patient renders evaluation of the precipitating factor difficult.

During the last two decades particularly, with the increasing use of chest x-ray examinations, many cases of spontaneous pneumothorax have been detected in apparently healthy persons with no symptoms, signs or roentgenographic evidence of tuberculosis or other pulmonary disease. Most cases have been observed in young men. The causative association, in the great majority of cases, between a so-called "idiopathic pleural effusion" and tuberculosis is still valid. Although the possible existence of a small subpleural tuberculous focus that is not demonstrable by roentgenography may be the source of a pneumothorax, accumulated data indicate that the old conception of the rigid relation between spontaneous pneumothorax and tuberculosis needs revision. Essential, idiopathic and primary spontaneous pneumothorax are terms that are designated as the pneumothorax of apparently healthy persons. Obviously, every case in which such a diagnosis is made should be carefully studied during and after complete re-expansion of the lung to rule out tuberculosis. If the disease has been excluded at the time, the patient is no likelier to develop tuberculosis later than the average person. Kjaergaard² observed only 1 case in a follow-up study of 49 patients after a two-year period. Perry,³ who re-examined 55 out of 85 patients without finding a single case of tuberculosis, stated that in 250 cases mentioned in the literature that were checked for several years only 6 patients had tuberculosis.

In our clinical material, 28 patients, or 72 per cent, definitely showed no clinical or roentgenologic evidence of tuberculosis either of the first or re-

infection type, and they can be grouped as cases of primary spontaneous pneumothorax. In 1943, among the Army population in the continental United States, there were 873 hospital admissions for this condition.⁴ The average hospitalization period was forty days. Approximately 15 per cent of the soldiers were separated from the service, and the remainder were returned to general or limited duty. Our figures conform closely to these. The most reliable criteria in differentiating a simple primary from a tuberculous spontaneous pneumothorax are negative clinical and roentgenologic evidence of tuberculosis, a negative tuberculin test, absence of adhesions, little or no fluid, absence of fever and prompt recovery with fairly rapid re-expansion of the lung.

The pathogenesis of primary spontaneous pneumothorax is explained on the basis of one of three main conditions or mechanisms.

Congenital cystic disease of lungs. There may be congenital maldevelopment of the bronchi and cystlike pulmonary anomalies. One or more of the cystlike dilatations may rupture and produce spontaneous pneumothorax.⁵

Rupture of subpleural emphysematous blebs. The most frequent site for these blebs is in the apexes and upper anterior margins of the lungs. The theory has been advanced that under conditions of increased intrathoracic pressure, such as that produced by coughing and sneezing, with the glottis closed, air is forced from the bases of the lungs into the apexes because of the less rigid nature of that portion of the chest wall.⁶ The process of repeated distention of the apexes ultimately causes a rupture of the elastic fibers in the walls of peripherally located alveoli. Air then escapes into the alveolar layer of the pleura, which becomes raised and separated from the alveoli. The air dissects itself along the pleura and is finally intercepted by the lobular septums. The mere presence of emphysematous blebs, however, does not necessarily augur the development of spontaneous pneumothorax. Positive autopsy evidence of blebs is often found in patients with a negative clinical history of spontaneous pneumothorax. This accident is attributed to a check-valve mechanism, which permits easy ingress but difficult egress of air from the subpleural bleb, so that the bleb becomes distended and thin walled and finally ruptures, with or without an element of physical exertion. Roentgenographic examination sometimes demonstrates in large blebs or vesicles a fluid level that constitutes indirect evidence of a check valve. Furthermore, at post-mortem examination, the air cannot readily be expressed from some blebs, whereas in others the procedure is comparatively easy. The check valve manifests itself as an expiratory obstructive mechanism in the form of inspissated exudate, scar tissue in

the region of the bleb and the adjacent bronchiole (Kjaergaard⁷ reported such a finding at autopsy in 2 nontuberculous patients) or openings between the bleb and the communicating narrowed alveoli that may be of different sizes.⁸ Emphysematous blebs are sometimes seen in the roentgenograms of the chest, usually in the apexes, and appear as thin-walled ring shadows that simulate tuberculous or bronchiectatic cavities. The absence of surrounding reaction and the lack of clinical symptoms and signs constitute the chief differential features. It should also be stated that thoracoscopy — direct inspection of the pleural cavity in the presence of pneumothorax — may reveal emphysematous vesicles, the best objective ante-mortem evidence is furnished by this procedure.

Rupture of interstitial emphysematous blebs. McGuire and Bean,⁹ Hamman¹⁰ and Macklin¹¹ believe that this is a plausible mechanism. Macklin, in experimental animal studies, found that by increasing the intrapulmonary pressure, air escapes from small ruptures in the walls of alveoli or bronchioles and then traverses the perivascular sheaths through the interstitial tissue to the root of the lung, where it pierces the mediastinum and produces spontaneous mediastinal emphysema, dissects along the fascial planes in an upward or downward direction, or both, — and thus causes a more or less generalized emphysema, — or extends to the pleura forming a bleb that ruptures. Miller¹² recently described 4 cases of spontaneous mediastinal emphysema, 2 of which were associated with a pneumothorax. The simultaneous bilateral spontaneous pneumothorax that occurs in some idiopathic cases is probably due to a rupture in the portion of the posterior mediastinum, between the esophagus and aorta, in which the two layers of mediastinal pleura are in contact. Macklin and Macklin¹³ suggest that there may be a constitutional or hereditary factor — an inherent weakness of the alveoli and the pleura — which predisposes to rupture. In support of this hypothesis, they refer to reported cases of spontaneous pneumothorax occurring in the same families, in most of whom there was no demonstrable pulmonary pathology, tuberculous or otherwise, to account for the pneumothorax.

Therapy

Additional remarks on treatment are pertinent.

The immediate treatment of spontaneous tuberculous pneumothorax consists in complete bed rest, relief of shock, if present, symptomatic medication for cough, nervousness and so forth, aspiration of air or fluid, or both, from the pleural cavity to relieve cardiac or respiratory distress and oxygen therapy. A spontaneous pneumothorax should be converted into a therapeutic pneumothorax if the underlying pulmonary disease warrants its mainte-

nance If, after a reasonable period, the affected lung shows little or no tendency to re-expand, the possibility of a bronchopleural fistula should be investigated This condition was present in one of our tuberculous patients with a tension pneumothorax, and underwater drainage was instituted, with considerable relief of dyspnea

Most patients with primary spontaneous pneumothorax require no treatment except partial or complete bed rest for a few weeks Symptomatic treatment, oxygen therapy and aspiration of air are applicable when indicated The immediate prognosis in unilateral cases is excellent Recurrent pneumothorax is not infrequent, however Its incidence, of course, depends to some extent on the length of the follow-up period of observation Four of our cases, or 10 per cent, were recurrences Wilson¹⁴ reported 20 per cent, and Ornstein and Lercher⁶ 30 per cent Recurrences in any given patient cannot be foretold in advance and cannot be prevented except by the obliteration of the pleural space by adhesions This can be artificially produced, but should not be undertaken after the first episode of spontaneous pneumothorax because the majority of patients suffer only one attack, following which they engage in moderate or strenuous exertion for years with no recurrence Waring¹⁵ discusses the problem of inducing a chemical pleuritis, by the injection into the pleural cavity of an irritant, such as sterile mineral oil or Gomenol, to create pleural synphysis

Military Disposition

The disposition, which is not always uniform for any given condition, varies with Army directives, the medical installation in which hospitalization occurs, the particular type of duty performed by the soldier and so forth The disposition of patients with nontraumatic spontaneous pneumothorax from a medical point of view depends largely on the etiologic diagnosis Patients with cases secondary to pulmonary tuberculosis (reinfection type) should be discharged from the service

In primary spontaneous pneumothorax, the underlying pathologic process is benign Whether the exertion of military duties is an increased hazard remains an open question A history of strenuous physical effort, as an exciting cause, is lacking in many cases It would be interesting to obtain data on the comparative incidence of primary spontaneous pneumothorax and its correlation with physical activity among civilians and military personnel of the same age groups The chief precautionary measure for these patients is the avoidance of exertion, coughing or straining with a closed glottis, which increase intrapulmonary pressure and may precipitate a spontaneous pneumothorax, provided the appropriate anatomic background exists Holter and Horwitz¹⁶ also cautioned against airplane travel for persons with a diseased pleura

They reported a case in which the spontaneous pneumothorax was interpreted as being due to the change in atmospheric pressure by ascent to 8000 feet They believed that the fall in pressure from 760 to 560 mm of mercury increased the tendency for pulmonary collapse, exploited a pleural weakness (emphysematous bleb) and produced a spontaneous pneumothorax This conclusion was disputed by Engel and Ferris,¹⁷ who in commenting on the case report, stated that the pneumothorax existed prior to or was coincidental to the flight rather than being caused by it, and that the reduction in barometric pressure is transmitted equally and promptly to all body tissues so that the ratio between the intrapulmonary and intrapleural pressures remains the same Their explanation was as follows

Changes in pressure and volume will occur only in gas containing structures that have inadequate or no communication with the external atmosphere (i.e., middle ear, paranasal sinuses, gastrointestinal tract) As long as there is no air in the pleural space there will be no relative change in intrapulmonary pressure and hence no tendency for the lung to collapse partially Similarly an emphysematous bleb would not be any more likely to rupture at altitude unless it had little or no communication with intrapulmonary air

Probably the most frequently recommended military disposition is reclassification of the soldier to limited duty after an episode of unilateral primary spontaneous pneumothorax and separation from the Army for patients with recurrent unilateral or simultaneous bilateral collapse This policy has not been consistently followed at this installation

SUMMARY AND CONCLUSIONS

Forty-one soldiers with nontraumatic spontaneous pneumothorax were admitted to a large army hospital during a four-year period (1941-1944) The pertinent military data concerning the incidence, length of service and hospitalization and disposition are presented

In 39 cases there was sufficient information for evaluation of the clinical and roentgenologic aspects The most important single clinical feature was the correlation between physical exertion and pneumothorax, in 60 per cent of the cases the episode was unassociated with exertion, in 26 per cent physical effort was mild and not related to military activity, and in 13 per cent exertion was severe and linked directly to military duties The main roentgenologic observation was the presence of underlying active pulmonary tuberculosis in 5 per cent, inactive reinfection disease in 76 per cent, calcified primary infection in 10 per cent and no parenchymal disease in 77 per cent of the cases

Primary spontaneous pneumothorax is the pneumothorax of apparently healthy persons with no clinical or roentgenologic evidence of pulmonary disease Its pathogenesis may be due to rupture of a congenital pulmonary cyst or to a subpleural

or interstitial emphysematous bleb. The differential diagnostic criteria and the therapeutic measures in tuberculous and primary spontaneous pneumothorax are briefly discussed.

The military disposition depends largely on the etiologic diagnosis. Soldiers with pulmonary collapse attributable to tuberculosis (reinfection type) should be discharged from the Army. Primary spontaneous pneumothorax is benign. The disposition most frequently recommended is reclassification to limited military duty following an attack of pulmonary collapse and separation from the service following simultaneous bilateral or recurrent unilateral episodes.

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PLASMA ALPHA AMINO NITROGEN LEVELS IN PATIENTS WITH THERMAL BURNS*

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INCREASES in the concentration of plasma amino acids following burns have been reported by Glenn, Muus and Drinker¹ in calves, and by Harkins and Long² in rats. The present communication reports a study of the plasma alpha amino nitrogen concentration in human beings with extensive burns.

METHODS

Twelve patients with severe burns admitted to the Boston City Hospital during the period 1943 to 1945 were studied. The essential details are summarized in Table 1. The area of burn was estimated by the method of Lund and Browder,³ and the depth of burn classified according to the method of Converse and Robb-Smith.⁴ These authors classify the depth of burn by name instead of by degree, using the terms "epidermal" for burns with erythema only, "dermal" and "deep dermal" for superficial and deep injury of the derma without complete destruction, and "deep" for burns with complete destruction of all epithelial elements. In this study the area of

epidermal burn was disregarded. The depth of burn cannot be determined with accuracy in patients who survive for only a few days, and consequently can only be approximated. The local treatment was dry, sterile, pressure dressings with no preliminary cleansing. Anesthesia was not given, the dressings being done under mild morphine sedation.

The alpha amino nitrogen concentration was determined by the ninhydrin method of Van Slyke.^{5,6} The determinations were usually made on plasma and occasionally on serum, care being taken to avoid delay in separation of the blood cells.

A preliminary study of the method was made on fifty blood samples from 9 normal persons. The mean value for all determinations was 3.6 mg of alpha amino nitrogen per 100 cc of plasma, with a standard deviation of 0.36 mg from the mean. The criterion for significant elevations over normal in the patients under study was a concentration of alpha amino nitrogen at least three times the standard deviation above the normal mean value — that is, a level of 4.7 mg of alpha amino nitrogen per 100 cc of plasma was considered significantly elevated.

All the patients received homologous plasma in amounts varying from 0.5 to 6.5 liters during the first forty-eight hours. To rule out the possible effects of plasma administration on alpha amino nitrogen concentration in the plasma, 2 normal subjects were given 1.5 liters of two-year-old liquid plasma in the course of two hours. Serial determina-

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tions of plasma alpha amino nitrogen concentrations before, during and at hourly intervals after the administration of plasma showed no significant changes.

Hemoglobinemia was found in almost all samples during the first twenty-four hours. About 15 per cent of the circulating red blood cells, however,

fall in the plasma alpha amino nitrogen concentration below normal. In contrast, 8 of the 12 patients showed a significant elevation of the plasma or serum alpha amino nitrogen concentration in the first twenty-four hours following injury. Seven of these 8 patients had burns, chiefly deep, involving over 35 per cent of the body surface, whereas 1 (Case 1)

TABLE 1 *Clinical and Laboratory Data on Patients with Severe Burns*

CASE No.	AGE	SEX	EXTENT OF BURN		PERIOD AFTER BURN	SHOCK	PLASMA ALPHA AMINO NITROGEN	QUICK PROTHROMBIN TEST*	HEMOGLOBIN	PLASMA NONPROTEIN NITROGEN	VOLUME OF URINE†	RESULT
	yr		TOTAL %	DEEP %	hr		mg/100 cc		%	mg/100 cc	cc	
1	42	F	15	10	3 1/4 4 1/4 13 27 51 120	Present Present Present Absent Absent Absent	4.9 4.2 4.8 3.5 2.9 2.8	21/21 — 22/22 26 5/25 5	90 90 74 84 71 56	28 32 36 31 32 21	1100 (first day) 1100 (second day) 2500 (third day) 4215 (fourth day) 2500 (fifth day)	Recovered
2	12	F	20	5	1 2 4 8 12 14 24	Absent Absent Absent Absent Absent Absent Absent	3.9 3.7 3.3 3.8 3.9 3.5 4.2	— — — — — — —	93 92 90 90 99 102 113	28 30 32 28 33 29 —	900 (first day)	Recovered
3	75	M	20	6	3 8 12 18 24	Absent Absent Absent Absent Absent	4.1 3.8 2.8 3.7 3.5	18/20 18/20 — 18/20 —	100 93 91 99 98	20 22 23 26 30	600 (first day)	Recovered
4	83	M	35	++	2 4 10 13	Present Absent Present Absent	4.8 4.9 5.9 5.6	20 5/17 — — —	102 102 88 86	36 50 43 64	Low (first day)	Died after 22 hr
5	78	M	35	++	2 6 10 12 1/2	Present Present Present Absent	7.6† 5.7 6.5 6.1	28/24 5 30/24 5 29/24 5 33/24 5	129 118 132 120	35 36 — —	105 (16 hr)	Died after 16 hr
6	29	M	35	++	1 4 6 13	Absent Present Present Absent	4.3 4.8 6.1 5.7	— — — —	141 172 169 152	29 29 40 51	1145 (first day)	Died after 22 hr
7	33	M	40	+++	2 13 22 1/2 120	Absent Absent Absent Absent	4.0† 3.1 3.1 3.1	21/24 5 27 5/24 5 — —	108 115 96 —	23 28 24 —	340 (first day) 1240 (second day) 2675 (third day) 5730 (fourth day) 3760 (fifth day)	Died on 10th day
8	8	F	50	++	3 5 1/4 13 19 28	Present Absent Absent Absent Absent	4.3 3.6 4.4 3.1 2.7	21 5/23 20 5/23 22/23 25/24 27/24	135 110 112 87 86	34 36 46 55 41	196 (first day) 540 (second day)	Died on 3rd day
9	38	F	50	+++	2 7 9 1/4 14 20 25	Absent Absent Absent Absent Absent Absent	3.8 4.2 4.4 4.4 5.3 4.5	— — — — — —	83 112 106 112 111 91	20 28 35 46 63 62	200 (first day) 858 (second day) 150 (third day)	Died after 63 hr
10	45	M	60	+++	3 1/4 4 11 1/4 13 1/4 3	Absent Absent Present Present Present	5.2 5.3 6.1 6.1 5.8	21/22 5 26/22 5 25 5/22 5 — —	120 127 130 44 89	27 32 44 — 20	70 (16 hr)	Died after 16 hr
11	3	F	70	+++	1 7 1/4 13 1/4 22 1/2	Absent Absent Absent Present	4.4 5.7 5.1 6.7	24 5/25 30 5/25 27 0/25 26 0/25	126 127 125 118	26 37 46 58	458 (first day)	Died after 30 hr

*The second figure represents the value of the normal control

†Determination on serum instead of plasma

‡The figures in parentheses represent the period during which the sample was collected

would have had to have been destroyed to account for a rise of the plasma alpha amino nitrogen concentration to the levels considered significantly elevated in this communication. Hemolysis of such a degree did not occur.

RESULTS

The over-all data obtained in the 12 patients are listed in Table 1. In no case was there a significant

had 15 per cent of the body surface burned. The elevation of the plasma alpha amino nitrogen concentration in this last case was transitory and not so great as that in the others.

Clinical shock was present in varying degrees in 7 of the 8 patients. Four of these patients had marked hypotension on entry, and in all the plasma alpha amino nitrogen concentration was elevated at that time. In the other 3 patients hypotension occurred

four, eleven and a half and twenty-two hours, respectively, after entry, in the last 2 patients the plasma alpha amino nitrogen concentration was elevated before the period of hypotension, whereas in the other the elevation occurred for the first time at the time of hypotension. In four patients the level remained high for varying lengths of time after the shock had been successfully treated.

There were 4 patients with no significant elevation of the plasma or serum alpha amino nitrogen concentration, 3 of whom had no shock at any time. The extent of burn was 20 per cent in 2 of these patients and 40 per cent in the other. Another patient, an eight-year-old girl, was severely burned, 50 per

hours after injury, at about which level it remained until death on the third day. Icterus indexes in the other patients in the twenty-four hours after entry were unsatisfactory because of the presence of hemoglobinemia. Later determinations were available only in 1 patient (Case 1) with an elevation of the plasma alpha amino nitrogen, and were normal. Icterus indexes were also normal in the 4 patients who had no significant elevation of the plasma alpha amino nitrogen concentration.

The quick prothrombin time was prolonged in 4 of the 5 patients with elevated plasma or serum alpha amino nitrogen concentration on whom the determinations were made, but were not significantly

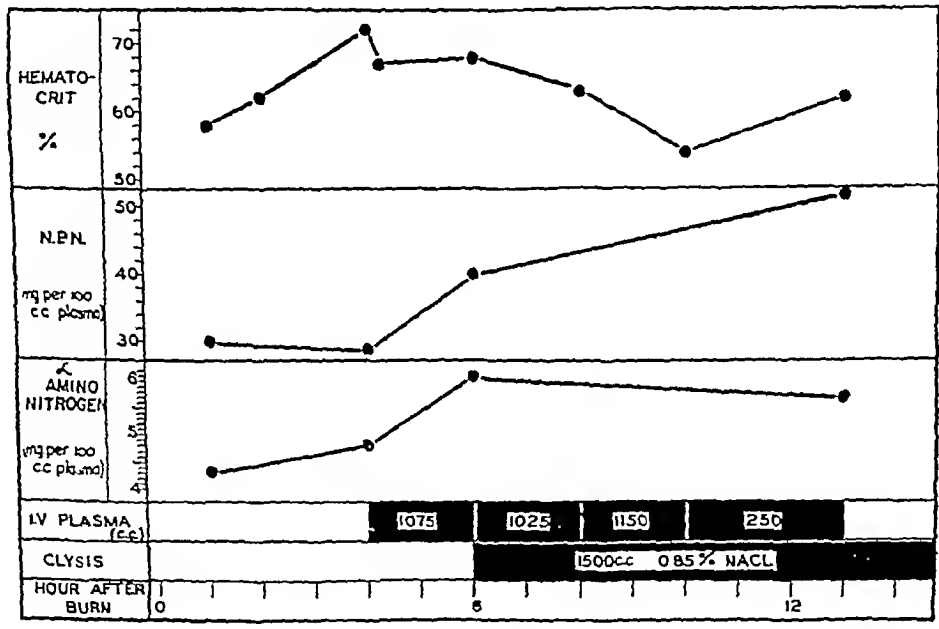


FIGURE 1 Case 6

cent of the body surface being involved. Shock was severe on entry but thereafter was minimal or absent.

In the 8 patients with significant elevation of the plasma alpha amino nitrogen concentration, 7 showed an elevation of the nonprotein nitrogen of the plasma above 35 mg per 100 cc. Oliguria was usually present in these cases. In all but 1 patient, however, the rise in the alpha amino nitrogen concentration was observed at times when the nonprotein nitrogen concentration in the blood was still normal. Hemoconcentration was present in almost all the 12 cases but was more marked in the 8 patients with increased alpha amino nitrogen concentrations.

No patient in this series had a history or physical signs of liver or renal disease. One patient (Case 9) was a morphine addict. The icterus index in this patient was 10 on entry and rose to 25 within seven

prolonged in 3 patients with no significant elevation of the plasma alpha amino nitrogen.

Post-mortem examinations were performed on 5 patients who had had significant elevations of plasma alpha amino nitrogen concentration and on 2 who had not. In no case were significant hepatic morphologic changes found.

The following case reports typify the findings in the group of patients showing an increased plasma alpha amino nitrogen concentration.

CASE 6 L. A., a 29-year-old man with a noncontributory history, sustained flame and electric burns and some damage to the respiratory tract shortly before entry. Thirty-five per cent of the body surface was involved in mixed dermal and deep burns, chiefly the latter. The data are presented in Figure 1.

Examination on entry revealed a well developed and well nourished man. The blood pressure was 130/70, the pulse 100 and of good quality, and the respirations 25. The hemo-

globin was 141 per cent, and the alpha amino nitrogen concentration 4.2 mg per 100 cc of plasma.

During the next 3 hours small amounts of water were administered orally, no other fluids being given. The patient gradually went into profound circulatory collapse, no blood pressure or pulse being obtainable for the last half hour of this period. The extremities were cold, clammy and cyanotic. There had been no output of urine. The hemoglobin had risen to 172 per cent, whereas the plasma alpha amino nitrogen concentration had risen slightly — to 4.8 mg per 100 cc. Administration of plasma was then begun, and during the next 2 hours the systolic blood pressure was kept between 80 and 90 and was thereafter above 100. The pulse improved in quality, and the extremities were no longer cold, clammy or cyanotic.

The plasma alpha amino nitrogen had risen to a level of 6.1 mg per 100 cc 5 hours after entry and continued elevated during the next 7 hours. The plasma nonprotein nitrogen concentration, which had been 30 mg on entry, was 40 mg per

culatory collapse, as well as a slight rise in the serum alpha amino nitrogen concentration to 6.2 mg per 100 cc. There were progressive hoarseness and respiratory distress, and the patient died of respiratory failure 16 hours after injury. Autopsy revealed no significant hepatic morphologic changes.

DISCUSSION

The data show that in most patients with extensive deep burns there was a significant elevation of the serum or plasma alpha amino nitrogen concentration in the first twenty-four hours after injury. This was observed in 7 of 8 patients with burns, chiefly deep, involving 35 per cent or more of the body surface. Marked hemoconcentration and clinical shock were present in all but 1 of these pa-

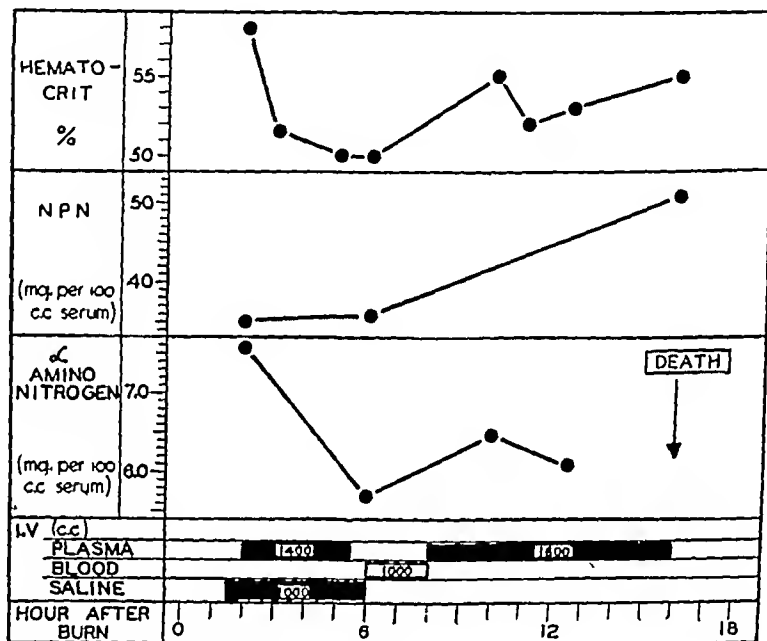


FIGURE 2 Case 5

100 cc at the peak of the alpha amino nitrogen rise and continued to rise to a level of 50 mg per 100 cc. The patient had occasional periods of respiratory distress, which were relieved by intravenous aminophyllin. The temperature was about 103.5°F.

Twenty-four hours after injury the patient suddenly died from respiratory failure. Autopsy revealed no significant hepatic morphologic changes.

CASE 5 F M, a 78-year-old man with a noncontributory history, received flame burns of 35 per cent of the body surface shortly before entry. The burns were mixed dermal and deep. Some damage to the respiratory tract had also been sustained. The data are presented in Figure 2.

Examination on entry revealed an elderly, apathetic man, with cold, clammy, cyanotic extremities. The blood pressure and pulse were not obtainable. The hemoglobin was 129 per cent, the nonprotein nitrogen 35 mg per 100 cc of serum, and the serum alpha amino nitrogen concentration 7.6 mg per 100 cc. Plasma, whole blood and normal saline solution were given intravenously. The hemoglobin varied between 118 and 132 per cent, and the nonprotein nitrogen rose to 50 mg per 100 cc of serum. The serum alpha amino nitrogen fell from the initial level of 7.6 to 5.8 mg per 100 cc 4 hours later. During this period the blood pressure and pulse were satisfactory. Thereafter, there were 2 brief periods of cir-

culation. In some patients, however, the rise in plasma alpha amino nitrogen was observed before the onset of hypotension, and in others the elevation persisted after the blood pressure returned to normal. These findings are similar to those reported by Hoar and Haist⁸ following tourniquet injury to rats. Elevation of the serum alpha amino nitrogen concentration has also been reported from this laboratory⁹ in patients with so-called "medical shock." The correlation of increased alpha amino nitrogen with the severity of shock was marked in these cases.

An increased nonprotein nitrogen concentration in the blood plasma was usually observed in the patients in the present series. In all but 1 case, however, the rise in plasma alpha amino nitrogen concentration occurred at a time when the nonprotein nitrogen concentration was still normal. It has previously been reported from this laboratory¹⁰ and elsewhere¹¹ that protein catabolism proceeds at a very

gh rate in patients with extensive burns. It has generally been accepted¹² that a rise in the over-all nitrogen turnover in the body does not lead to an increase in the plasma alpha amino nitrogen concentration, but when the rate of nitrogen metabolism is markedly increased and the liver is not functioning normally, there is probably some rise in the plasma alpha nitrogen.¹³ Although there is no direct evidence that abnormalities of liver function existed in this series of patients, it is likely that some disturbance was actually present. This is suggested by the elevation of the Quick prothrombin time in most cases. Engel et al¹³ and Wilhelm and his associates¹⁴ have shown in animals that hepatic function is abnormal during hemorrhagic shock, and have specifically demonstrated that the ability of the liver to deaminate amino acids is impaired. Thus, hyperaminoacidemia is probably related to a combination of an increased production of amino acids and a decrease in the rate of deamination by the liver. This view has also been expressed by Engel et al,¹³ Hoar and Haist⁸ and Wilhelm and his associates¹⁴ to account for the rises in plasma alpha amino nitrogen observed in shocked animals.

SUMMARY

Plasma or serum alpha amino nitrogen concentrations were elevated in 8 of 12 patients with thermal burns.

There was a close correlation among the elevation of the plasma alpha amino nitrogen concentration, the extent of the burn, the degree of shock and the prolongation of the Quick prothrombin time.

In some cases the elevation of the alpha amino nitrogen occurred before marked hypotension was present, and persisted after the blood pressure returned to normal.

The rise in plasma alpha amino nitrogen concentration occurred before that in the nonprotein nitrogen concentration.

It is postulated that hyperaminoacidemia is the result of an increased production of amino acids, together with a decrease in the rate of deamination by the liver.

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globin was 141 per cent and the alpha amino nitrogen concentration 4.2 mg per 100 cc of plasma.

During the next 5 hours small amounts of water were administered orally, no other fluids being given. The patient gradually went into profound circulatory collapse, no blood pressure or pulse being obtainable for the last half hour of this period. The extremities were cold, clammy and cyanotic. There had been no output of urine. The hemoglobin had risen to 172 per cent whereas the plasma alpha amino nitrogen concentration had risen slightly—to 4.8 mg per 100 cc. Administration of plasma was then begun, and during the next 2 hours the systolic blood pressure was kept between 80 and 90 and was thereafter above 100. The pulse improved in quality, and the extremities were no longer cold, clammy or cyanotic.

The plasma alpha amino nitrogen had risen to a level of 6.1 mg per 100 cc 5 hours after entry and continued elevated during the next 7 hours. The plasma nonprotein nitrogen concentration which had been 50 mg on entry, was 40 mg per

cent, as well as a slight rise in the serum alpha amino nitrogen concentration to 6.2 mg per 100 cc. The patient died of respiratory failure 16 hours after injury. Autopsy revealed no significant hepatic morphologic changes.

DISCUSSION

The data show that in most patients with extensive deep burns there was a significant elevation of the serum or plasma alpha amino nitrogen concentration in the first twenty-four hours after injury. This was observed in 7 of 8 patients with burns, chiefly deep, involving 35 per cent or more of the body surface. Marked hemoconcentration and clinical shock were present in all but 1 of these pa-

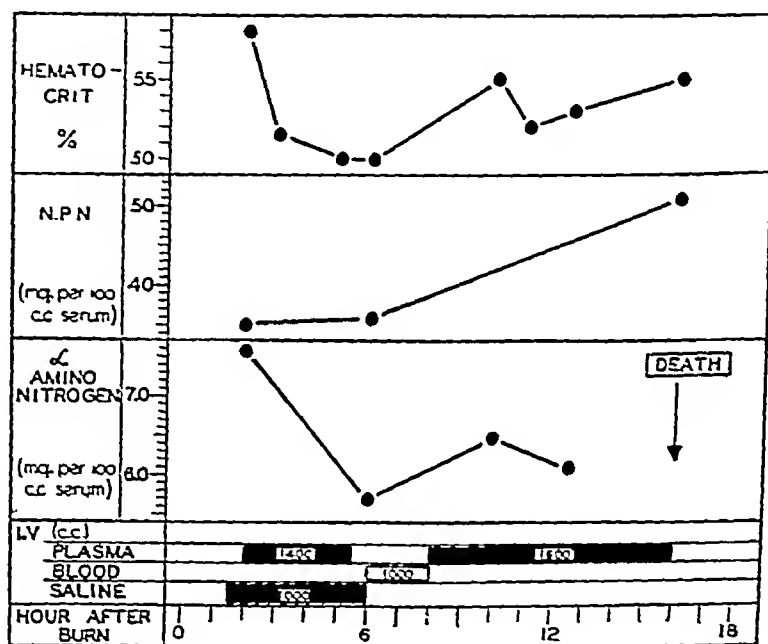


FIGURE 2 Case 5

100 cc at the peak of the alpha amino nitrogen rise and continued to rise to a level of 50 mg per 100 cc. The patient had occasional periods of respiratory distress which were relieved by intravenous aminophyllin. The temperature was about 103.5°F.

Twenty-four hours after injury the patient suddenly died from respiratory failure. Autopsy revealed no significant hepatic morphologic changes.

CASE 5 F M, a 78-year-old man with a noncontributory history, received flame burns of 75 per cent of the body surface shortly before entry. The burns were mixed dermal and deep. Some damage to the respiratory tract had also been sustained. The data are presented in Figure 2.

Examination on entry revealed an elderly, apathetic man, with cold, clammy, cyanotic extremities. The blood pressure and pulse were not obtainable. The hemoglobin was 129 per cent, the nonprotein nitrogen 35 mg per 100 cc. of serum, and the serum alpha amino nitrogen concentration 7.6 mg per 100 cc. Plasma, whole blood and normal saline solution were given intravenously. The hemoglobin varied between 118 and 132 per cent, and the nonprotein nitrogen rose to 50 mg per 100 cc. of serum. The serum alpha amino nitrogen fell from the initial level of 7.6 to 5.8 mg per 100 cc 4 hours later. During this period the blood pressure and pulse were satisfactory. Thereafter, there were 2 brief periods of cir-

culatory collapse, as well as a slight rise in the serum alpha amino nitrogen concentration to 6.2 mg per 100 cc. The patient died of respiratory failure 16 hours after injury. Autopsy revealed no significant hepatic morphologic changes.

In some patients, however, the rise in plasma alpha amino nitrogen was observed before the onset of hypotension, and in others the elevation persisted after the blood pressure returned to normal. These findings are similar to those reported by Hoar and Haist⁸ following tourniquet injury to rats. Elevation of the serum alpha amino nitrogen concentration has also been reported from this laboratory⁹ in patients with so-called "medical shock." The correlation of increased alpha amino nitrogen with the severity of shock was marked in these cases.

An increased nonprotein nitrogen concentration in the blood plasma was usually observed in the patients in the present series. In all but 1 case, however, the rise in plasma alpha amino nitrogen concentration occurred at a time when the nonprotein nitrogen concentration was still normal. It has previously been reported from this laboratory,¹⁰ and elsewhere¹¹ that protein catabolism proceeds at a very

important in the dispute over the question whether allergy of dermatophytosis predisposes to the development of contact dermatitis. Both groups included that it did not. These two statements are contrary to our experience in private industrial practice and to the opinion expressed by Neal and Anmons.⁴⁴ Examinations in offices and at plants showed that less than 5 per cent of workers demonstrate clinical evidence of fungous infections. We so believe that the role of cutaneous sensitization is well established. The mere presence of dermatophytids on the hands produces sites of lowered resistance sufficient to break the skin and allow the mechanical and chemical contacts of industry to aggravate the original eruption.

Conant et al.⁴⁵ describe a long list of mycotic infections, of which the following may be classed as attributable to occupational contacts. Actinomycosis is found in agricultural workers and is twice as frequent in men as in women. North American blastomycosis is presumably not contagious but has been acquired by direct contact, the cases reported being those of a physician infected while performing an autopsy and an infant infected from a cutaneous lesion on the arm of a nurse. The sex ratio is 9 males to 1 female, and the disease is found mostly among the poorer classes. Coccidioidomycosis is an infection carried in the soil and by wild rodents, laborers are likelier to develop the severe form than workers in other occupations, and laboratory workers become infected by inhaling spores from dried cultures. A recent study of the primary form of this disease in Army camps showed that 0.2 per cent of the cases developed into a progressive and fatal form. South American blastomycosis also occurs in a ratio of 9 males to 1 female, the disease develops most frequently in manual laborers whose work is of such a nature that vegetative material is brought into contact with the skin. Chromoblastomycosis affects the laboring classes almost exclusively. Moniliasis causes lesions of the hands in housewives, bakers, waiters, bartenders and fruit packers whose hands are macerated by frequent soaking in water. Sporotrichosis is apparently acquired from plants, although it may be contracted from infected animals. The disease occurs oftener in men than in women, especially in farmers, laborers and horticulturists. Maduromycosis is also more frequent in men than in women, in 100 cases cited by Bocarro,⁴⁶ 91 of 92 men were farmers and 7 of 8 women were wives of agriculturists. Aspergillosis is an infection occurring in persons often exposed to massive doses of spores, as in squab feeders who take grain onto their mouths to moisten it, fur cleaners who use rye flour as a grease remover and agricultural workers exposed to dust from threshing machines. Certain species of mucoromycosis produce epidemics of paronychia among orange workers. Rhinosporidiosis has been reported only 13 times in the United States, the disease develops in persons who swim or dive in

stagnant water and is frequent among the sand divers of India.

Insect Infestations

Saunders⁴⁷ reports 2 cases of workers handling straw who developed an itchy eruption. Examination of the straw revealed tyroglyphid mites. The cutaneous manifestations were excoriated urticarial papules, splotchy erythema and intense itching of the neck, face and forearms.

Dermatitis from fowl mites occurring in 2 persons in the same household is reported by Knotts.⁴⁸ *Dermanyssus gallinae* was identified as the cause. The patients' clothing was infested with these mites while they were gathering eggs, tending chickens and cleaning the coops. The bites on the skin became papules with pruritus, which on scratching became excoriated and then crusted. Such patients complain of nocturnal itching, because these mites bite at night. This condition is confused with scabies, but the presence of mites on the clothing, the lack of burrows and the patient's occupation serve to differentiate the two conditions.

In a review of occupational dermatitis,³² so-called "grocer's itch" occurring in handlers of dried fruits is mentioned. Dried dates, figs, prunes, apples and pears are sometimes infested with mites known as *Carpoglyphus passulorum* and *Glyciphagus domesticus*. Tea leaves are sometimes infested with a mite known as *Rhizoglyphus parasiticus*, and wheat may contain a mite known as *Aleurobius farinae*.

CHEMICAL AGENTS

The group of chemical agents causing dermatoses is a large one, comprising the acids, alkalis, salts, hydrocarbons, crude coal-tar products and other organic compounds.

Acids

Schwartz⁴⁹ reports an unusual form of occupational dermatitis that occurred in a plant manufacturing hydrochloric acid. The outbreak occurred after a change was made in the manufacturing process, consisting in the addition of 0.4 per cent of soft coal to the salt briquets from which the acid was made. One of the towers in which hydrochloric acid gas was absorbed by water was cleaned out, and all of 13 men thus engaged developed dermatitis after coming into contact with a yellow, waxy deposit on the fan. Eight months later 27 men who cleaned out another tower also developed dermatitis. The eruption began with itching and burning, and edema of the face and eyelids. After the eruption had subsided, there remained comedones, pustules and acnelike cysts. Patch tests with the waxy substance, which contained 5 per cent hydrochloric acid by weight, were positive. This is a primary irritant.

MEDICAL PROGRESS

OCCUPATIONAL DERMATOSES (Concluded)

J G DOWNING, M D,* AND S J MESSINA, M D †

BOSTON

VITAL AGENCIES

Bacterial Infections

Lebowich, McKillip and Conboy³⁷ report 3 cases of cutaneous anthrax. All the patients were working in leather tanneries, where they handled imported skins. After an average incubation period of one to three days they developed anthrax of the skin, which began as a single, small, red papule on an exposed surface that enlarged rapidly, with development of a central necrotic brownish-black eschar surrounded by a pink, doughy swelling and pink vesicles. No pain was experienced but a sense of fullness and numbness at the site of infection. The constitutional symptoms were persistent headache, fatigue and weakness and also fever.

Ecthyma contagiosum, which is an infection frequent in animals, is reported by Kingery and Dahl³⁸ as occurring in a farm worker who treated sheep for so-called "fluke disease." The animals' mouths were forcibly opened, and in this process the fingers were traumatized. Many of the animals had scabs or pustular lesions on the lips. Three lesions developed on the right thumb, and there were similar ones on the fingers of each hand. The lesions, which were firm papules or papulovesicles on an erythematous base, cleared within a week with mild treatment.

Mycotic Infections

One of us (J G D³⁹) has shown that persistent eruptions on the hands, frequently labeled fungous infections by industrial physicians and inexperienced dermatologists, are usually due to secondary infection by pyogenic organisms. Ayers and Anderson⁴⁰ state that without confirmatory evidence a diagnosis of fungous infection of the hands stands an 88 per cent chance of being wrong. A positive diagnosis can be made only through laboratory evidence.

The hands and feet of 406 patients with a contact dermatitis of more than three months' duration were examined by a trained mycologist working under the supervision of one of us (J G D³⁹), because it is often said that fungus is a secondary invader and prolongs contact dermatitis. Direct microscopic examination of scrapings showed fungous infection on the hands of 5 patients, and cultures showed infection on the hands of 2.

Superficial and deep-seated mycotic infections affect workers. When fungi are regularly found in

an occupational contact, it is reasonable to assume that the worker suffering from organisms peculiar to his labor has an occupational disease. Among workers exposed are those who till the soil or come in contact with plants, hay, straw and animals and their by-products, such as feathers, silk, wool and leather. Kennel keepers acquire microsporosis. Dairymen and herders suffer from trichophytosis due to an ectothrix. Dermal moniliasis occurs in bakers, preserve packers, fruit handlers, salad makers and dishwashers. Deep-seated infections are usually found in farmers, cattlemen, florists, horticulturists, wood handlers and research workers. In Massachusetts primary fungous occupational infections are comparatively rare, but industrial physicians should not only know the fungi to which the worker is exposed but also be trained to prepare and to recognize cultures of fungi.

The most striking report of recent years is that of du Toit⁴¹. In South Africa in 1927 sporotrichosis made its appearance in the gold mines of the Witwatersrand when 14 native workers were found to be suffering from infections due to *Sporotrichum beurmanni*. In 1941, 74 cases were reported in two other mines. All these patients were timber boys. From the middle of 1941 to February, 1942, a total of 650 cases of sporotrichosis was found in an underground shaft where 2500 natives were employed. The epidemic then began to spread among European workers. The company accepted responsibility on the assumption that the disease always followed injury, no matter how insignificant it might be. The clinical types occurring in the mines included the classic lymphangitic type, seen in America, and the multiple ulcerative type, seen in France. The infection was undoubtedly brought into the mine by a native from the tropical east coast. The fungus was isolated from the air and timber in the mines. Treatment, which was simple and effective, consisted of large doses of potassium iodide by mouth, to a total of 200 gm.

Peck and his associates believe that dermatophytosis and its allergic manifestations are not an important factor in lost time among industrial workers.⁴² In the report of the Council on the Treatment and Prophylaxis of Dermatophytosis,⁴³ based on the work of the United States Public Health Service, it is stated that it appears reasonable to assume that more than 50 per cent of persons in industry are affected by dermatophytosis, but it is also affirmed that the evidence of Peck and his associates is most

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A drum containing the compound burst, igniting the clothing of a girl employed in unloading drums. The flames were soon extinguished, but the portion of the skin in contact with the sodamide suffered severe burns. The patient died the next day. Autopsy showed acute fibrinotic inflammation of the larynx, trachea and bronchi and many local second-degree burns on the skin.

Methyl Bromide

Butler, Perry and Williams⁵⁶ report a case in which 2 men whose boots were in contact for five hours with methyl bromide, a fire-extinguisher fluid, developed large blisters of the feet. Wyers⁵⁷ calls attention to the symptoms of toxicity of this compound. Brief exposure to the gas caused headaches, smarting of the eyes, cough, loss of appetite, abdominal discomfort and numbness of the feet. Methyl bromide is used in industry as a methylating agent, for refrigeration purposes, as a fumigant and for the control of rodents and fleas. The liquid form rapidly penetrates the clothing, even boots and rubber covering. The characteristic skin lesion is a large blister.

Zinc Chromate

Hall⁷ reports that of 132 persons sensitive to zinc chromate primer, 90 (68 per cent) were sensitive to zinc chromate only. The average duration of exposure before the eruption developed was seven months. Nummular eczematous plaques or groups of papules appeared on the radial and flexor aspects of the wrists, the dorsal aspects of the proximal portions of the thumbs and the volar and ulnar aspects of the forearms.

Lead Arsenate

Monahan⁵⁸ reports an unusual case in which a laborer handling bales of dried pumice in a vinegar factory developed contact dermatitis from the dust, which showed a strongly positive qualitative test for arsenic. It was found that the apples whose peelings were used in the manufacture of vinegar had been sprayed with lead arsenate before being dried.

Vinyl Carbazole

Exposure to vinyl carbazole, according to Tabershaw and Skinner,⁵⁹ resulted in dermatitis in two plants, where the compound was used in manufacturing electric equipment. It is employed in the polymerized form after 98 per cent pure carbazole is treated with acetylene under heat and pressure and filtered, purified and dissolved in monochlorobenzene in the presence of a catalyst. The white amorphous substance is insoluble in water but soluble in chlorinated hydrocarbons, petroleum hydrocarbons and fats.

Tricresyl Phosphate

Gaul and Henneger⁶⁰ report a case of dermatitis bullosum produced in the seborrheic areas of the

body by contact with tricresyl phosphate which was used as a substitute for plasticizer for adhesive tape. The dermatitis was not found in the area of contact, but disappeared on removal of the tricresyl phosphate and recurred when further patch testing was done. The authors stress the significance of a chemical that can invade unbroken skin and produce cutaneous lesions indistinguishable from established disease patterns of seborrhea.

Trichlorethylene Gas

A case of widespread dermatitis due to the inhalation of trichlorethylene gas is reported by Baker and White.⁶¹ There have been no previous reports in the literature of such dermatitis from the inhalation of vapor. A foreman whose office was twenty feet from a degreasing unit suffered diffuse erythematous eruptions of the entire body. The lesions disappeared when he was away from his work but reappeared on his return. When he wore a gas mask no dermatitis occurred, but when he failed to wear it severe burning and pruritic eruptions developed within a few hours. One of us (J G D) had a patient who on exposure to trichlorethylene developed a herpetic eruption of the face and loss of sensation of taste.

Benzidine

Baer⁶² reports a recurrent pruritic eruption on the hands and face of a physician who performed benzidine tests on stool specimens. It recurred each day that he performed the test, the eruption starting on the fingers of the left hand. Patch testing showed benzidine to be the cause, benzidine powder producing an extremely strong eczematous reaction.

Explosives

The explosives causing most cases of dermatitis are tetryl, TNT (trinitrotoluol), fulminate of mercury, ammonium picrate and picric acid, smokeless powder, amatol, amonal, hexite, lead styphnate, sensol and lead azide. Nitroglycerin does not produce dermatitis but can be absorbed through the skin and cause cardiovascular disease.

Tetryl About 4 per cent of tetryl workers develop dermatitis,⁶ but most cases occur in the loading areas. Tetryl manufacture and pellet production are to some extent closed processes, which accounts for the small number of cases of dermatitis. Peck, Gant and Schwartz⁶ report higher percentages of tetryl workers developing dermatitis. Allergic dermatitis is caused oftener by tetryl than by any other explosive.^{19, 63, 64} The eruption appears in newly employed workers within one or two weeks on exposed surfaces — on the face, hands and forearms — and secondarily where dust collects — on the wrists, back of the neck, ankles and feet. The face, hair and hands are stained yellow. Associated symptoms are epistaxis, dryness of the throat and cough.

TNT Sensitization dermatitis is produced by TNT but not so frequently as by tetryl. The derma-

Alkalies

An eczematoid eruption affecting the back of the hands and the flexor surface of the forearms is reported by Whitwell⁵⁰ as arising from the carbonizing of steel. During this process organic carbonizers are mixed with sodium bicarbonate or barium carbonate and the impregnated pellets are packed by hand around the steel. The cause of the dermatitis is the sodium bicarbonate in the pellets, which even after being washed are still strongly alkaline. The barium carbonate is not so harmful. The rash developed after workers had been thus employed for several months. Such workers should do no carbon packing when they are sweating or when their arms are wet after washing, otherwise they soon have a strong solution of soda on their skin.

Dural

Hall⁷ reports 10 cases of dermatitis due to dural, representing 5 per cent of 202 cases of occupational dermatitis in aircraft workers. Dural is an alloy composed of 95 per cent aluminum, 4 per cent copper, 8.5 per cent each of manganese and magnesium and traces of iron and silicon. The eruption consists of scattered pale-pink, fine papules, usually excoriated and covered with sanguinous crusts. The lesions are located on the forearms. In 1 of these cases they were on the flexor surface of the wrists, the sides of the neck were affected in half the cases. The hand and fingers were not involved. Each of the patients showed a slight or moderate reaction to patch tests with dural drillings. The duration of exposure before evidence of sensitization appeared averaged slightly over five months.

Aluminum

In this same series Hall⁷ encountered 4 cases of dermatitis due to aluminum. Each patient showed a slight reaction to aluminum filings. This eruption is evanescent and may disappear within twenty-four hours away from work. The lesions are wheal-like and erythematous, appearing on the forearms, wrists, face and neck. The average duration of exposure is four and a half months.

Selenium Dioxide

Selenium dioxide is used extensively in the electric industry. Workers with pure selenium did not develop skin trouble, but those working with the dioxide compound had typical reactions.⁵¹ A crystal of selenium dioxide under the fingernail produces a painful reaction lasting for about two days. The pain then subsides somewhat, and a small red spot remains. This is followed by a small scar in the area. In severe cases necrosis develops in areas of contact with this compound. There is a burning sensation, intolerable at times. In the series reported, patch tests with pure selenium produced no reaction, but those with selenium dioxide caused such severe reactions that the patches were removed after a few

hours. The reactions were painful, and vesicles developed at the site tested, with eventual deep necrosis. This report proves the danger of patch tests with chemicals that are undoubtedly primary irritants.

Cobalt

Cemented carbides are made from tungsten, tantalum and titanium carbides, carbon and metallic cobalt. In a plant manufacturing these materials, 20 men who had worked in the metal room for a month or more before developing dermatitis were examined.⁵² The eruption was erythematous and papular. Some lesions were ringed, with clear centers, appearing on the cubital spaces, the sides of the neck, the eyelids, the flexor aspects of the forearms and the backs of the hands. In 2 workers who swept the dust from the floor, patches of dermatitis appeared on the external malleolus and ankle. Patch tests on 6 workers showed negative reactions to oxides of tungsten, tantalum and titanium and to carbon but positive reactions to metallic cobalt and to the black powder containing all the metals. Two controls, not working in the plant, gave negative reactions to all metals and thus showed that this is a sensitivity dermatitis. Some of the workers developed tolerance and were able to continue in this work.

Silver

In a case of argyria reported by Wigley and Deville⁵³ the black pigmentation of the skin was due to constant exposure to silver nitrate.

Beryllium

In the last four years, 170 cases of beryllium poisoning have been seen in three plants.⁵⁴ The manifestations included dermatitis, chronic skin ulcers and inflammatory changes in the respiratory tract. The severest manifestation was a diffuse pneumonitis, which caused the death of 5 workers. In the processing of ore, beryllium oxide is extracted under a high temperature from crushed inert ore beryl by acids and fusion methods. Fumes and dust encountered at various steps in this process were the cause of the poisoning. Contact dermatitis and skin ulcers occurred in 42 workers, usually accompanied by rhinitis and nasopharyngitis. The dermatitis occurred within a week after starting work involving contact with beryllium sulfate, beryllium fluoride or beryllium oxyfluoride. The eruption, which was edematous and papulovesicular, occurred on the hands, arms, face and neck, with intense itching. Ulcers were caused by a beryllium crystal deposited in the skin, a small indurated papule resulted and progressed to necrosis. Early excision and curettage of the site afforded complete healing.

Sodamide

A case of acute sodamide poisoning with a fatal result is reported by Pozhariskii and Khodzhash.⁵⁵

with rubber or some other material prevented dermatitis

MISCELLANEOUS CASES

Sterling⁷² reports a severe dermatitis of four years' duration in a waitress. The areas affected were the flexor surfaces of the forearms and the fingertips, the fingers were either split or showed oozing crusted patches. A germicidal powder known as Microlene was found to be responsible, the patient having handled dishes washed in this chemical solution.

Nine cases of contact dermatitis in a morphine factory were reported by Dore, Thomas and Green.⁷³ The average period between the beginning of employment and the appearance of dermatitis was fourteen and a half weeks. The eruption began as an irritating erythematous dermatitis of the eyelids, sometimes with edema. The nape of the neck and the area below the chin were next involved in women, and the collar area in men. The specific sensitizer was not found.

According to Goodman,⁷⁴ cold-wave "permanents" affect the molecular structure of the skin as well as the hair. This is a simple chemical reaction, not an allergic one. Thioglycolic acid should be suspected when one encounters a dermatitis consisting of erythema, vesicles, fissures, pustules, lichenification and itching of the hands of workers dealing with cold-wave fluids. Commenting on an article by Cotter,⁷⁵ however, McCord⁷⁶ makes the following observations: there is no primary skin irritation from thioglycolic acid or alkaline derivatives at levels below 8 per cent and no evidence of sensitization and allergic responses with properly prepared materials under any circumstances, hydrogen sulfide formation can be controlled through stabilization, and no measurable systemic responses occurred in his tests on animals after parenteral introduction.

A baker complaining of a skin eruption of one year's duration was found to be sensitive to benzoic acid in the improved flour he was using.⁷⁷ When he substituted nonimproved flour, the dermatitis, which affected the hands, neck and chest, rapidly disappeared. A patch test with 6 per cent benzoic acid in liquid petrolatum gave a positive reaction.

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titis chiefly affects the hands. The cutaneous manifestations are edema, papules and deep-seated vesicles, especially on the palms.¹⁹ Other regions frequently affected include the wrists, forearms, neck creases and feet.⁶⁴ The face is rarely involved. There is considerable staining of the hands.

Fulminate of mercury This explosive, which is more sensitive than tetryl and is used in detonators and primers, causes ulcers of the skin if it enters abrasions and also sensitization dermatitis.¹⁹ The eruption appears first on the backs of the hands and the forearms as erythematous lesions, which tend to remain discrete, and on the face as erythema, with edema of the eyelids and also conjunctivitis.⁶⁴ The irritation develops on the fourth to the sixth day of contact.

Ammonium picrate and picric acid These explosives are used as bursting charges. They cause yellow discoloration of the skin and hair and a sensitization dermatitis of the face.¹⁹

Smokeless powder This powder contains dinitrotoluol or diphenylamine, which produces a sensitization dermatitis.

Synthetic Rubber

When the sources of natural rubber were cut off, there was a tremendous increase in the manufacture of synthetic rubber. This process involves several compounds that cause irritation and sensitization dermatitis among workers. Types of synthetic rubber made in this country are buna S, buna N, butyl rubber and neoprene. Comparatively little dermatitis occurs in the manufacture of synthetic rubber, despite the many irritant chemicals employed.⁶⁵ This is explained by the facts that factories are now equipped with mechanical safety devices and that most of the chemical processes are closed. The various compounds used and their effects are as follows.

Butadiene The vapors of this compound are irritating to the eyes, nasal passages, throat and lungs.⁶⁶

Tertiary butyl catechol This compound is an inhibitor, preventing butadiene and styrene from polymerizing while in storage. It is a skin irritant and causes sensitization dermatitis.¹⁹ ⁶⁵

Styrene This is also a skin irritant and sensitizer.⁶⁵

Phenylbetanaphthylamine This antioxidant is a skin sensitizer.⁶⁵

Hydroquinone This compound is usually added to the latex. It is a cause of sensitization dermatitis.⁶⁵

Aluminum chloride This chemical, which is a catalyst, is a skin irritant.⁶⁵

Bardol This is a coal-tar derivative and is both a primary irritant and a photosensitizer.¹⁹ ⁶⁵

Chlorobutadiene This liquid causes erythema of the skin from splashes, even if immediately washed off with water.⁶⁵

Acrylonitrile This compound is extremely toxic, both from vapor inhalation and from toxic absorption. It may cause dermatitis.⁶⁵

Soapstone This substance is used to cover bales of rubber. If it is coarsely powdered its handlers develop dermatitis, especially during the hot months.⁶⁵

Rubber Goods

Mercaptobenzothiazole This accelerator was found to be the most frequent cause of sensitization dermatitis.⁶⁷

Rubber gloves Three cases are reported of physicians who wore rubber gloves and developed itch and dermatitis.⁶⁸ Neoprene gloves were substituted for ordinary latex and were tolerated.

MILITARY CASES

A temporary sensitivity that was specific for woolen clothing has been reported in members of the Canadian Army who had previously been treated several times for scabies with lotions whose principal ingredient was benzyl benzoate.⁶⁹ Two separate lotions were used, but this compound was the only substance common to both and each lotion produced the same result. Patch testing with wool and cotton showed sensitivity to wool only. In no case was the period between use of the lotion and development of wool sensitivity less than two weeks. In some cases discharge from the military service was necessary. This dermatitis should be distinguished from recurrence of scabies.

Dermatitis from contact with a Navy identification tag has been reported.⁷⁰ After forty-eight hours contact with one of these tags, which are made of chrome steel, a steward's mate developed pruritus, burning, marked erythema and vesicles. There was no history of allergy other than urticaria following the ingestion of grapefruit or lemon. The original contact was with the wrist, but the ankle and neck reacted similarly when brought into contact with the tag. The lesions, which developed after two weeks of contact, lasted for over eighteen months. There were no generalized symptoms of chrome poisoning. Excessive sweating may have resulted in greater solubility of chromates as a factor in this sensitivity. No case of this kind had previously been reported.

Dermatitis from the wearing of Army spectacles has been reported.⁷¹ Six cases were seen within three months at a clinic in Scotland. The frames were made of an alloy of nickel, zinc and copper. Patch tests with pure nickel and with alloy plated with nickel gave positive reactions. Tests showed that under conditions of wear in the presence of perspiration and body heat the dissimilar metals of the alloy can set up an electrolytic action and give rise to an allergic phenomenon. In all cases removal of the spectacles brought rapid clearing of the lesions. All the patients but 2 had pityriasis sicca capitis and perspired freely. Prausnitz-Küstner tests were negative, probably because the subjects did not sweat enough. Covering of the spectacle frames

with rubber or some other material prevented dermatitis

MISCELLANEOUS CASES

Sterling⁷² reports a severe dermatitis of four years' duration in a waitress. The areas affected were the flexor surfaces of the forearms and the fingertips, the fingers were either split or showed oozing crusted patches. A germicidal powder known as Microlene was found to be responsible, the patient having handled dishes washed in this chemical solution.

Nine cases of contact dermatitis in a morphine factory were reported by Dore, Thomas and Green.⁷³ The average period between the beginning of employment and the appearance of dermatitis was fourteen and a half weeks. The eruption began as an irritating erythematous dermatitis of the eyelids, sometimes with edema. The nape of the neck and the area below the chin were next involved in women, and the collar area in men. The specific sensitizer was not found.

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facts regarding the industrial exposure, and last comes a good measure of common sense. If a worker's hands are wet during the greater part of his working hours, if he is constantly exposed to irritation from fumes and dusts, if an epidemic of eruptions appears in a group of workers, if the skin is splashed with a primary irritant, and if the clothes are soiled for hours with a volatile solvent such as gasoline, it requires no great learning to assume that the worker is suffering from an occupational dermatitis. Careful history taking limits the possible factors, and proper application of a few patch tests solves the problem when the history of the irritating factor is not too evident.

THE PATCH TEST

Patch testing consists in putting a portion of the material to be tested on the subject's skin and covering it first with linen and next with a larger piece of adhesive or other impervious material. Although the actual technic is simple, knowledge of when to perform the test, with what materials and in what dilution presents a problem for the expert. Serious consequences can follow the test. Primary irritants should not be used, since some of them are also sensitizers. The latter, in the proper dilution, can be tested. Textbooks usually give tables for guidance. As a rule, products made for wear can be tested full strength or as they are.

It must be realized that because patch testing cannot simulate all the actual conditions of exposure — sweating, friction and other factors to which a worker is subjected — its value is limited. It is an aid in the diagnosis of occupational dermatosis. A recent questionnaire on patch tests⁸⁴ supports the view that although these tests have their limitations, they are of definite value. During a twelve-month period, for example, Howell⁸⁴ was able to prove the exact cause of 250 cases of contact dermatitis by patch-testing with the suspected materials.

Patch-test reactions are recorded as follows: a + reaction shows definite erythema, a ++ reaction shows erythema and papules, a +++ reaction consists of vesiculation, and a ++++ reaction shows a denuded area at the site of contact. A preplacement patch test on the skin is carried out with materials or chemicals that a worker comes in contact with on his job. The advantages of this test enumerated by Keil⁸⁵ consist in eliminating cases of latent hypersensitiveness, placing a person in the right industry and determining whether a substitute chemical should be used. The following objections have been raised to this type of testing: a person may be sensitized to the material tested, he may sue, he may have a positive reaction and yet show no clinical evidence of dermatitis, and evidence of sensitization is not always a sure indication that the worker will suffer a dermatitis. It has been proved that many workers, such as bakers who have never had a cutaneous eruption, react to patch tests

with substances to which they are exposed. Again, many workers handle sensitizers for twenty years or more before suffering from a cutaneous disturbance. In still other cases those who continue their work and subsequently become immune or less susceptible are shown by patch tests to be still sensitized, but are able to maintain tolerance to their exposures.

So-called "prophetic patch testing" is done with the purpose of foretelling whether a substance will or will not produce a dermatitis.⁸⁶ The test is made on 200 or more persons in the usual way. Since the chemicals to be tested are new ones, it is assumed that there has been no contact with them. Two series of patch tests are carried on in the same subjects ten to fourteen days apart. The first series give reactions to primary irritants or produce them in persons previously sensitized, and the second show how many subjects have been sensitized by the first series.

LEGAL ASPECTS

In Massachusetts an occupational dermatosis may be defined in the words used by one of the courts in describing personal injury as "any injury, damage, harm or disease of the skin which arises out of or in the course of employment." Such an injury is compensable if it causes incapacity and takes away a worker's ability to earn wages.

No one is better qualified to decide the diagnosis, the differential data and the etiologic factor than the dermatologist. When specialists disagree, an impartial and duly qualified dermatologist is appointed to examine and report, and his report is considered admissible as evidence, provided that the employee and the insurer have been seasonably furnished with copies of it (General Laws of Massachusetts, Chapter 152, Section 9). The employee who is unable to employ a dermatologist always has the right to an impartial examination.⁸⁶

On October 14, 1935, the Massachusetts Legislature adopted an amendment to permit a claim of industrial disease to be referred to three impartial physicians, who are allowed to examine the patient, investigate working conditions as they deem necessary, and report to the Industrial Accident Board their diagnosis and opinion regarding the cause and extent of incapacity, if any. The report must be made by a majority vote of the referees. The diagnosis should be positive — that is, it should specify the disease or condition found or state specifically that no disease was found. This report is binding and final, but the Board can base its decision on the previous history or on subsequent facts. The diagnosis of the medical referees must be made from the physical signs present at the time of examination, although this diagnosis may be made months after the onset, perhaps when the patient has recovered. As a result, interesting complications have developed. The constitutionality of this statute has been extensively debated. There is no doubt

at it has prevented an employee from having a complete or full trial on his claim of industrial disease when the Industrial Accident Board appoints the three physicians. On the other hand, he is saved the expense of employing one or more experts to testify in a questionable case.³

In April, 1946, the provisions of the Workmen's Compensation Act that provide for the appointment of three medical referees who hold *ex parte* investigations and make reports binding on the Industrial Accident Board were declared unconstitutional by the full bench of the Massachusetts Supreme Judicial Court. The decision, written by Justice James J. Ronan, declared that the 1935 law, amended in 1938, "deprives a party of his fundamental rights" under both state and federal constitutions.

The question of cancer of the skin arising from a single injury is a cause of frequent legal and medical disputes. Such claims as the following are constantly appearing. A thirty-four-year-old man was struck by a splinter from an emery wheel, which penetrated his cheek. Probing for the splinter led to considerable trauma, followed by swelling and suppuration. The swelling became larger and harder. Two months later it measured 1.5 by 2.0 cm and appeared as a sharply defined lesion with a verrucous center, with no pain. Removal and histologic examination revealed a prickle-cell carcinoma.⁴⁷

Perhaps owing to the employment of older workers during the manpower shortage, one of us (J. G. D.) has seen a large increase in the number of workers making claims for skin cancer arising from a single injury or an industrial exposure. Many of these claims present evidence of a slight blow that has received first-aid treatment. Most blows have been on the face, the frequent site of cutaneous cancer in old age. Careful examination and the history of the original injury would have shown that a cancer was already there and that the trauma had caused bleeding at a site where an intact skin would have shown no evidence of injury. This sequence of injury, continued treatment and final recognition of a cancerous growth, together with inept or biased medical testimony, presents facts that few industrial commissioners have the temerity to dismiss.

Whether or not a fatal or disabling cancer was caused by an industrial accident is certainly a question not of law but of fact. If reasonable evidence has been introduced in the proceedings before an industrial board to sustain a finding that an industrial injury, single or multiple, has caused a cancer that resulted in disability or death and the Board so decides, an appellate court in any state in which the general rule laid down above is in force cannot set aside the award or remand the case for further proceedings, even though the court believes that the weight of all the evidence did not justify the decision. In any event, so long as the cause or

causes of cancer are not known, so long as there is an opinion among the medical profession at large to the effect that a single trauma may cause cancer, and so long as physicians are willing to testify under oath that in their professional opinion the disability can and did occur in the case under consideration, the industrial commission cannot be blamed if it sometimes accepts such evidence and grants awards accordingly. In forming his opinion in a given case, the physician should bear in mind the lack of definite knowledge regarding the relation of a single injury to the causation of cancer.

Whether human cancer can be caused by a single accidental injury remains an open question, the results of clinical observations are not conclusive. Although authentic cases are recorded in which cancer arose at the site of injury, the possibility that it was under way before the injury or developed independently of it cannot be excluded. That cancer can and does arise independently of injury and that single injuries become associated with cancer in one way or another in extremely few cases cannot be denied. So far as is known, cancer in animals has not been produced experimentally by a single mechanical injury.⁴⁸ Stewart⁴⁹ states "As far as I know, I have never seen a cancer which I could logically and irrevocably assign to single trauma and, even more important than that, I do not know that anyone has observed the development of a process which could be called 'precancerous' after a trauma."

TREATMENT

There is nothing new to be said about treatment, but it is necessary to reiterate that the use of antibiotics, such as penicillin, or of new bactericidal or fungicidal chemicals has no place in the treatment of uncomplicated industrial dermatoses. Despite the fact that some workers become immune to their contacts, there is no question that when a worker suffers an occupational dermatitis, the sooner he is removed from his work the speedier his recovery will be. The physician should use only soothing remedies, such as wet dressings, lotions and bland ointments.⁵⁰ A valuable new contribution, however, is the use of BAL (British anti-lewisite) in the treatment of cases of chronic arsenical and mercurial poisoning, certain physicians have also been trying it on other industrial cases.⁵¹

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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIFTH
ANNIVERSARY

House of Delegates, May 13 and 14, 1946 (Concluded)

Dr Sycamore then assumed the chair, while Smith presented his report as delegate to the House of Delegates of the American Medical Association

The 1945 session of the American Medical Association was curtailed to a meeting of the House of Delegates, which was held in Chicago on December 3, 4 and 5. Your delegate served on the Reference Committee on Reports of Officers. To expedite the work of the Association and express its policies more promptly, it was voted to hold two meetings of the House of Delegates each year. It was decided that the next session would be held in July, 1946, in San Francisco, and plans were developed for the centennial meeting at Atlantic City in 1947. You are all urged to attend this momentous meeting.

Dr George R. Minot, of Boston, was awarded the Distinguished Service Award, and Dr Harrison H. Shoulders, of Nashville, Tennessee, was elected president-elect. The Section on General Practice of Medicine was established. Dr Roger I. Lee delivered two excellent addresses, which have been published in the *Journal of the American Medical Association*, emphasizing the democracy of the House of Delegates. County medical societies through the state societies and their delegates bring items of business and express their opinions at the meetings. Perhaps our society has been lax in this respect, for your delegate has been instructed only once during the years that he has served.

The sudden end of hostilities and the rapid demobilization of medical officers created such a demand for even the increased number of residencies that, unfortunately, some physicians were unable to obtain them. The same conditions, together with the continuation of the accelerated program in the medical schools, prevented the inauguration of as complete a plan of postgraduate instruction as had been anticipated. You are referred to the *Journal of the American Medical Association* of December 22, 1945, for the details of the excellent work of the Committee on Postwar Medical Service.

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- 88 Editorial Workmen's compensation for cancer ascribed to an injury *J A M A* 125 1043, 1944
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NEW HAMPSHIRE MEDICAL SOCIETY

PROCEEDINGS OF THE ONE HUNDRED AND FIFTY-FIFTH ANNIVERSARY

House of Delegates, May 13 and 14, 1946 (Concluded)

Dr Sycamore then assumed the chair, while Smith presented his report as delegate to House of Delegates of the American Medical Association

The 1945 session of the American Medical Association was curtailed to a meeting of the House of Delegates, which was held in Chicago on December 3, 4 and 5. Your delegate served on the Reference Committee on Reports of Officers. To expedite the work of the Association and express its policies more promptly, it was voted to hold two meetings of the House of Delegates each year. It was decided that the next session would be held in July, 1946, in San Francisco, and plans were developed for the centennial meeting at Atlantic City in 1947. You are all urged to attend this momentous meeting.

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- 71 Taylor, W. O. G., Ferguson, A. G., and Arkiss, W. R. G. Dermatitis from wearing army spectacles, with special report. *Br J J* 2 40-42, 1945.
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The chairman was active in formulating requests for the return to civilian practice of physicians who were badly needed in their respective communities. He is pleased to report that a large number of physicians have considered coming to New Hampshire to practice, and many have already done so. He has answered at least fifty letters of inquiry and interviewed over thirty-five doctors. Although there are still several opportunities in the State for physicians, the areas in the greatest need are now supplied with medical care.

DEERING G. SMITH, *Chairman*
HAROLD I. L. LOVERUD
ANTHONY E. PETERS

Dr. Lewin, for the Committee on Officers' Reports, moved that the Committee on Medical Preparedness be discontinued, and that the by-laws be so changed. This motion was duly seconded.

A member inquired whether all men in the service had returned to civilian life.

Dr. Smith replied that two or three doctors who had been practicing in New Hampshire before the war were still in the service.

The motion was carried.

Dr. Smith then assumed the chair.

Dr. John P. Bowler then presented the following report:

Report of the Committee on Medical Education and Hospitals

During the last year, as in previous war years, there has been a general suspension in the activities of postgraduate training, particularly along the lines of the Commonwealth Fund, which has not resumed its subsidization of postgraduate fellowships.

The New England Postgraduate Assembly will renew its program this fall. This had been successfully operating as a two-day meeting at Cambridge for several years previous to 1942, and committees are now active in preparation for the re-establishment of what was on its way to being an obviously successful venture.

The Speaker's Bureau as operated by this committee principally for the supply of Society members for county meeting programs has continued, but in lesser demand than previously. Until now, when returning men will have made the medical personnel of the State more stable, no circularizing of the membership has been done for the enrollment of volunteers as speakers. Soon this will be undertaken, and a new list accumulated.

Senate Bill 191, which provides for a survey of hospital and health facilities within the various states to provide data for later consideration of federal grants toward the costs of construction of such facilities as needed, has led to the appointment of the New Hampshire State Commission for Hospital Study. This body, which was appointed by the Governor last summer, consists of fifteen members, with Mr. James M. Langley, of Concord as chairman. The medical representation on this commission includes Drs. George C. Wilkins and Jules Gagnon, of Manchester, Dr. Philip McQuesten, of Nashua, Dr. John P. Bowler, of Hanover, and the secretary of the Board of Health. The Governor and Council appropriated \$3000 for the purposes of this commission in the carrying out of its studies.

The State Department of Health has co-operated with the commission in preparing the health-center portion of the study. The State Planning and Development Commission has provided the office quarters, and its director has served as secretary to the commission, directing the work of the field representative, Mary T. Swoboda.

JOHN P. BOWLER, *Chairman*
JAMES W. JAMESON
SAMUEL M. BROOKS

Dr. Lewin, for the Committee on Officers' Reports, recommended that the delegates from the different county societies remind their secretaries that speakers for their various county meetings are available through Dr. Bowler's committee, and moved the acceptance of this portion of the report. This motion was duly seconded and was carried.

Dr. Lewin, for the Committee on Officers' Reports, then moved that the report of the Committee on Medical Education and Hospitals be accepted. This motion was duly seconded and was carried.

Dr. John B. McKenna then presented the following report:

Report of the Committee on Mental and Social Hygiene

I must plead guilty to procrastination in the matter of the report of the committee. Undoubtedly you are aware of the fact that Dr. Baker was to have made this report, but because of his retirement and emigration from New Hampshire, he suggested to Dr. Smith that one of the other members of the committee present the report. The third member of the committee, Dr. Simon Stone, had only recently returned to Manchester, and Dr. Smith therefore asked me some time ago to do this.

To begin with I cannot do much better than forward Dr. Baker's letter to Dr. Smith, in which there are incorporated several valuable suggestions with which I am in essential agreement. My difficulty in making such a report derives from the fact that, being peripherally located, I am not in sufficient contact with the more central problems. Therefore, my remarks can be the result only of essential experiences in connection with the more peripheral problems of psychiatry and mental hygiene in the State.

My first thought in this connection is that the field of psychiatry and mental hygiene in New Hampshire is peculiarly lacking in any effective co-ordination, because there is no one person in a position to do this co-ordination, such as the Commissioner of Mental Diseases in other states. Such a person and his assistants could more directly co-ordinate any efforts toward better psychiatric care and mental hygiene. I believe that under such a person Dr. Baker's suggestion regarding the formation of a state committee on mental hygiene could operate effectively in accordance with Dr. Baker's other suggestions. To these I add the desirability and practical necessity for more widespread use of psychiatric social-service workers, who might bring into contact many otherwise neglected cases of psychiatric problems with psychiatrists and mental hygienists. It has been my experience from practically ten years of psychiatry in the northern parts of New Hampshire, that there are many cases in which earlier psychiatric intervention might have forestalled more serious consequences. This would also imply the desirability of more peripherally located mental hygiene clinics, such as those existing in other parts of the State. Such additional clinics might well be located in places like Hanover and Littleton. Again, I have no basis for any knowledge of conditions in the more eastern parts of the state.

Some time ago, in a conversation with Dr. Dolloff, I brought up for discussion the possibility that the State could employ one or more psychiatric social-service workers whose duty would be to make periodic trips through the rural parts of the State to investigate and call to the attention of psychiatrists any specific needs for psychiatric help.

There is also an undoubted need for more widespread public education in psychiatric matters. In this connection it is worthy of note that the American Psychiatric Association has formed a committee on reorganization among whose proposed plans are included definite attention to organized programs for such education throughout the country. It might be well to look into this matter so far as New Hampshire is concerned, and I shall have definite information on this point after my attendance at the American Psychiatric Conference in Chicago later this

Dr Lewin, for the Committee on Officers' Reports, recommended that the House of Delegates establish a new standing committee, the New Hampshire Emergency Committee, consisting of three doctors formerly of the armed forces. This motion was duly seconded.

Dr Dye stated that if this were to be a standing committee the by-laws would have to be amended. The Secretary asked what the committee was to do. Dr Smith answered that the committee would try to find out what was wrong with the medical organization in the last war and prepare for the next war. A great many complaints and a great many criticisms, some constructive, had been received from medical officers and others who had served in the war. A number of the complaints had been turned over to this Committee of the American Medical Association, and it had accordingly been recommended that each state find other constructive items of criticism that could be used in the future.

Dr Dye suggested that the Committee on Officers' Reports, together with Dr Smith, draw up an amendment to be submitted for approval on the following day, in such a form that the name and duties of the committee would be specified in the by-laws.

Dr Smith stated the work of the committee could probably be accomplished in a year. It was to be like the Procurement and Assignment Service. All the criticisms that have arisen because of the participation of doctors in the war could be brought out, and constructive criticisms could be offered to the central committee of the American Medical Association, which, in turn, could be forwarded to the Secretary of War and the Secretary of the Navy, who were looking for criticisms.

The Secretary asked whether the Committee on Medical Preparedness could function in such a way. Dr Smith replied that the committee was to be composed of veterans.

The Secretary then inquired if a special committee for one year could take care of the situation. Dr Smith answered that it could.

Dr Lewin asked if the American Medical Association intended to have a national committee that would be permanent. Dr Smith did not believe so.

Dr Lewin, for the Committee on Officers' Reports, then moved that the House of Delegates create a committee, the New Hampshire Emergency Medical Service Committee, consisting of three doctors formerly of the armed forces during the war, to be elected by the House of Delegates for a period of one year or until the next annual meeting of the House of Delegates.

Dr Forsberg suggested that the motion be amended so that the committee would consist of five doctors. Dr Lewin accepted the amendment. This motion was duly seconded and was carried.

Dr Lewin stated the Committee on Officers' Reports had come to no conclusion on the question of

establishment of a bureau of information, but requested open discussion by the delegates.

The Speaker said that during the last year, he had received at least fifty letters and had interviewed over thirty-five physicians regarding moving to New Hampshire. Some of these men had visited New Hampshire. They wanted to know the best locations and what industries were to be found. He said that they were looking for residencies in all types of towns, in the various specialties. He had received letters addressed to the State Planning Commission, the State Board of Health, Dr Metcalf and Dartmouth College Medical School, all of which had been forwarded to him for reply. He believed that in the near future there would be many such requests, especially from men who had gone into the service directly from medical school. The whole effort had been to place these men in towns where no returning physician would be deprived of his practice, and also to attract them to the smaller towns and smaller areas, where there were no doctors. It had sometimes been difficult to interest these men in going to such areas. Dr Smith believed that a central clearing house should be set up, and suggested that the Secretary continue the work in the future, although he was already overworked.

The Secretary replied that he did not come in contact with the units mentioned, and that he did not know the towns very well. He stated that Dr Smith had been a godsend because he knew the situation at present. His only other suggestion was the State Board of Health, which received many requests for information.

The President called attention to the fact that the House of Delegates during the preceding year had created tentatively a committee for this particular purpose, with representatives from each county society. The men were to have been appointed by the county societies themselves, with a central chairman, and there would have been communication between the central chairman and the county-society members, each chosen for his temperament and his willingness and ability to serve as a local information agency from each county.

Dr Lewin, for the Committee on Officers' Reports, recommended that the Society co-operate to the fullest extent with any private prepayment plan of medical care, as a means of warding off a compulsory health program, and moved the adoption of this portion of the report. This motion was duly seconded and was carried.

Dr Lewin, for the Committee on Officers' Reports, then moved that the report of the delegate to the American Medical Association be accepted. This motion was duly seconded and was carried.

Dr Smith then read the following report

Report of the Committee on Medical Preparedness

The cessation of hostilities terminated the necessity of this committee during the past year, and it is recommended that it be discontinued.

the Committee on OPA Assistance be continued until the Government discontinues OPA through gressional action. This motion was duly seconded and was carried.

he report of the Committee on Public Health presented by the chairman, Dr Harris E Powers

The Committee on Public Health started out the year with the following members: Dr Harris E Powers, chairman, Dr Alfred Frechette, and Dr Anthony E Peters. During the course of the year, however, we had the misfortune of losing Dr Frechette, who accepted a call out of the State. New Hampshire and the New Hampshire Medical Society lost a very valuable man through this transfer.

In the previous year your committee had the pleasure of inspecting some of the lumber camps in the northern sections of the State, and this year conducted an inspection tour of the Portsmouth area, which has been one of the more concentrated industrial areas owing to the vast expanse in the Navy Yard during the war. On July 25, 1945, Dr Frechette, Dr McCloud, of the State Health Department, and your chairman proceeded to Portsmouth where we met Dr Peters. An inspection was conducted of one of the large milk plants in Portsmouth, and the method of handling milk from its entry into the plant, the processing of the milk and finally the bottling and preparation for delivery were covered. The pasteurizing of milk and the by-products, such as cottage cheese and ice cream, were followed through by your committee. The progress in the handling of milk in the past twenty years has been remarkable, but there is still room for improvement through the education of employees along sanitary lines. These efforts are being conscientiously carried out by the state health authorities.

From Portsmouth we followed along the South Shore to Seabrook, where the clam industry flourishes. Few people in the State realize the magnitude of this industry, and the small town of Seabrook seems to be the center of this activity. Scattered over the town are small shacks, which are used by the shuckers who receive the clams as they are dug and remove the meat from the shell. These individual industries are all small and few of them have anything like modern equipment. Of the many shacks that we inspected only one had stainless-steel benches, all the rest had wooden trays or benches. The process of shucking consists of removing the clams from the shells—this is all done by hand and with the aid of a short chisel-like knife, each clam is handled separately, the shell being cast in one pile and the clams being tossed in a container of one-gallon content. It was amazing to find that many of the clams had been dug from remote sections in Massachusetts and Maine, shipped to Seabrook in large barrels, shucked, and then transported back to wholesalers throughout New England. This is probably accounted for by the fact that the shuckers have established themselves in this community over a period of many years. They are a more or less isolated group, intermarrying generation after generation. The income of these employees seems adequate, and several of the workers said that they averaged six or seven dollars a day at their work. Their houses are extremely primitive, if the average laborer's house is used as a standard, and their customs and habits are equally singular. If their houses may be used as a guide they seem to have little interest in the niceties of life. The largest plant that we inspected employed ten to twelve people, the average being about six to ten employees. The State Health Department inspects these plants regularly for sanitary conditions and endeavors to improve the standards of the industry by screens on the windows, cleanliness in the shuckers themselves and boiling water and steam for sterilization purposes.

After inspecting the Seabrook area we proceeded to the Hampton Beach area. Some of the fire hazards were inspected and suggestions made, the proximity of the buildings at Hampton Beach result in a great fire hazard, and it is hoped that sufficient equipment will be retained at the beach to prevent such a catastrophe.

There is a great need in the communities that we inspected for education of both employers and employees along sanitary lines, particularly regarding handling of food supplies. It is certainly impossible for the Health Department to cover these territories as frequently as seems necessary with the small staff of inspectors available. It is one thing to make a suggestion and quite another to follow this suggestion up by routine calls to see that it is carried out. If sufficient inspectors were available to the Health Department to conduct these routine tours much more rapid progress and much better sanitary conditions would prevail.

Your committee has had no special problems turned over to it during the last year. We have endeavored to keep abreast with the work of other public health committees. It seems possible that, from time to time during the course of the year, your committee will conduct inspection tours of the various industries in the State similar to the one just described and will thereby keep a more active contact with the Health Department and industry throughout the State, submitting its report annually to the Society.

HARRIS E POWERS, *Chairman*
ALFRED FRECHETTE
ANTHONY E PETERS

Dr Lewin stated that during the national emergency, owing to the great shortage of labor, the practice of sanitation in restaurants, hotels, food stores and industries had been allowed to become alarmingly lax, and that Dr Powers had repeatedly referred to the shortage of public-health inspectors. Dr Lewin moved that the House of Delegates go on record as stating that the sanitation in the restaurants, hotels and the food handling industries of the State are lax. He also moved that the public-health laws of the State be more rigidly enforced, and that the Secretary send a note to the Health Department and to the Governor to that effect. This motion was duly seconded by Dr Sycamore.

The secretary inquired how effective such a step would be. Dr Wilkins replied that such action would probably do little good unless the Legislature could be induced to appropriate more money to hire more inspectors. The city boards of health did not have enough money to conduct all the inspections required by law. The remedy was up to the Legislature rather than to the Governor or the State Board of Health.

The President stated that it might be worth while for the delegates to pass a resolution voicing the opinion of the Society that larger appropriations were needed to make the proper personnel carry out the provisions already in the law.

Dr Sycamore asked if the matter should be referred to the Committee on Public Health. The President answered that the decision could be left to the discretion of the Secretary, who could send a note to the proper authorities. He moved that the Secretary send a note to the proper authorities. This motion was duly seconded and was carried.

Dr Lewin, for the Committee on Officers' Reports, moved that the Report of the Committee on Public Health be accepted.

This motion was duly seconded and was carried.

The report of the Committee on Tuberculosis was then presented by Dr Robert B Kerr.

month. At any rate, it seems obvious that the public enlightenment on psychiatric matters is a field that needs much more attention and can best be carried out by public talks throughout the State by accredited psychiatrists. This obviously implies the need for more well trained psychiatrists throughout the State. At the present time, to my knowledge, specialists in psychiatry outside Manchester and Concord are virtually nonexistent. Despite this fact there is a crying need for such specialists to share the burden of work, which is physically impossible for one or two persons. This indicates the advisability of taking some steps to attract well trained men to the State. In addition to the lack of mental-hygiene clinics, there is a strong need for facilities for the care of the mentally ill in the outlying parts of the State. It is well known that the State Hospital at Concord has been for many years tremendously handicapped by the fact that it is the only institution of its kind. Eventually some expansion of this institution or the erection of similar institutions in other parts of the State will be imperative. In the meantime, however, would it not be possible to establish, at one or more strategic points, modified institutions for the care and treatment of selected benign cases of mental disorder? In some such way the ponderous work of the present State Hospital could be materially reduced.

All these matters will necessarily require quite substantial financial expenditure. Whether or not this can all be taken care of by appropriations by the State is a matter with which I am quite unfamiliar. However, I should like to point out that the United States Government has before its consideration a bill providing for grants in aid to individuals, institutions and states throughout the country for the betterment of psychiatry in general. This should be looked into thoroughly, for I believe that this bill is likely to be passed and that New Hampshire is certainly one of the states in need of such assistance as might be afforded.

In summary, therefore, I believe that the primary need is for a co-ordinator in all psychiatric and mental-hygiene matters in the person of a director or commissioner of mental health, and that from such a department all the pertinent factors could be directed and co-ordinated and any relations with the United States Government could be established.

It is regrettable that this report must be in the nature of a theoretical discussion and not based on any statistical figures, but I believe that my distance from the central problems accounts for this lack. A further suggestion that might overcome such a deficiency is that future chairmen of the New Hampshire Committee on Mental Hygiene might be in more direct and more frequent contact with all the members of the committee, and that all might make a more active and statistical investigation of the requirements for satisfactory progress in this field.

JOHN B. MCKENNA

Dr McKenna then read Dr Baker's letter of March 6, 1946, to Dr Smith, as follows:

Dear Dr Smith

Yes! I am guilty. I resigned and retired and arrived here in San Antonio, Texas, on December 20, 1945. I sincerely hoped not to overlook my obligations but this matter being out of sight was also out of mind. I do not expect to return to New Hampshire before June 1. I do not have the addresses of my associates on the Committee or would write them at this late hour. Suggest you or Lewin write them of the situation and ask one of them to substitute for me.

My personal feelings are that we should get in touch with the National Committee for Mental Hygiene through its medical director Dr George D. Stephenson, 1790 Broadway, New York City, and get suggestions for forming a good strong committee for mental hygiene in New Hampshire. If this committee had an active president and secretary-treasurer and many active influential members willing to pay dues, it would be an agency for great good in New Hampshire. Perhaps it could include the present Social Hygiene Society. This committee could advise and co-ordinate public clinics and help support and influence public attitudes on mental health topics.

Then all state institutions should do what a small institution some years ago, the Laconia State School, did not have the courage or vision to do: put an item in the state institution budget to cover costs of mental hygiene clinics.

Clinics cannot be run for nothing. I think Dr Dolloff had funds left to that institution during the days of the Bancrofts. Father and son Massachusetts has many institutions. All these state institutions carry a heading for mental hygiene in their budgets, and the legislature allows it. If New Hampshire Medical Society approved such a course I am sure it would be a strong influence with the Committee on Appropriations.

I am sorry to be so lame in this matter but with the approval of other members of my committee, I recommend (1) that a New Hampshire Committee on Mental Hygiene be formed (2) that Dr George Stephenson be written to for assistance (3) that this committee advise and co-ordinate mental hygiene activities in New Hampshire (4) that the public on this subject, and (4) that all state institutions for mental defect, disease and derangement including the state school and state's prison, put an item in their budgets for extended mental hygiene work.

Sincerely,
BENJAMIN W. LEWIN

Dr Lewin, for the Committee on Officers' Reports, moved that the Committee on Mental Hygiene take the lead in this field of hygiene clinics, in educating both the public and the lawmakers. This motion was duly seconded.

Dr Clough inquired if the members of the committee could not provide, during the year to follow, a definite motion or program to be presented to the Governor of New Hampshire for funds to be raised for psychiatric clinics.

The President pointed out that there was great need in the State for outpatient psychiatric care and patient care for the people unable to meet the tremendous expense of the facilities available for private care. He therefore wished to hear from the members of the committee regarding a concrete plan for the State.

Dr Lewin, for the Committee on Officers' Reports, accepted the suggestion that the matter be turned back to the committee for a definite report at the next meeting. This was seconded, and the motion was carried.

The report of the Committee on OPA Assistance was then presented, as follows:

Report of the Committee on OPA Assistance

The District Food-Rationing Officer of the OPA called on your committee for advice regarding the need for additional unrationed foods in some hundreds of cases. As restrictions were removed on the sale first of processed foods and then of meats, these requests became less numerous. With the discontinuance of rationing, which we hope may come soon, this function of your committee will be at an end.

In deciding on the merits of so many applications, it has of course been necessary to be somewhat dogmatic. We have followed in the main the recommendations of the Subcommittee on Medical Food Requirements of the National Research Council, but we have tried to give a liberal interpretation.

Your committee early lost one member through removal to another state, and a second member was on duty outside New Hampshire during much of the year. This, together with the more urgent problems caused by rationing, prevented any effective consideration of the overall nutritional situation in New Hampshire. However, your chairman did discuss these matters with Miss Hinman, the state nutritionist, on two or three occasions. In more normal times, which we hope are at hand, such a committee could be of definite value in stimulating interest in good nutrition throughout the State.

There is as much "hidden hunger" in New Hampshire, especially in some rural areas, as in most other parts of the country. Stressing these problems and the best means of dealing with them, discussing them before the state and county medical society meetings and before nursing groups, as well as giving the state nutritionist every encouragement, should in the end be productive of definite results.

COLIN C. STEWART, Chairman
SIMON STOVE

Dr Lewin, for the Committee on Officers' Reports, moved that this report be accepted and

ork harder to be sure of continued reductions in the death rate. We appeal to the members of the Society for their continued aid and co-operation. We urge better and prompter reporting of tuberculosis cases by the practicing physicians to the State Board of Health. (The report slip states that the reports are confidential.) We suggest that the members of the Society request aid when it is needed in the examination of contacts and so forth. We urge further consideration of the practicability of routine chest x-ray examination of patients admitted to general hospitals. In this connection your committee hopes that in the coming year a plan may be worked out for such a study in one or two general hospitals in the State. The findings may be indicative of similar samplings elsewhere and may give more definite information regarding the possible values of such a procedure in New Hampshire.

ROBERT B. KERR, *Chairman*
RICHARD C. BATT

Dr Lewin referred to a point emphasized by Dr Kerr—the advisability of routine chest x-ray study of all patients admitted to general hospitals, but stated that the committee had recently consulted x-ray men and learned that film is still hard to obtain, so that the carrying out of this suggestion for the present seemed impracticable. He added that when x-ray film again became plentiful, however, one or two hospitals in the State should try routine chest x-ray examinations for a year, and the results should be reported at a future meeting of the House of Delegates.

Dr Lewin, for the Committee on Officers' Reports, moved that the House of Delegates go on record as favoring a one-year trial of routine chest x-ray study by two hospitals in the State when x-ray film again became plentiful. This motion was duly seconded.

Dr Sycamore stated that no difficulty in obtaining film had been experienced in his section of the State. He believed that the proposed study would be interesting, but that the question of its economic desirability would depend on the amount of unsuspected disease uncovered by such a survey.

The President asked who would be responsible for the cost of the study.

Dr Dye inquired what hospitals would be selected and by whom.

Dr Sycamore replied that these matters could be worked out by the New Hampshire Tuberculosis Association.

Dr Johnston stated that several Boston hospitals had carried out surveys, which had proved satisfactory.

Dr Clough expressed his belief that the State Hospital could carry out the study.

Dr Sycamore said that the State Hospital was a special type and that perhaps its study would not have as much value as one conducted by a general hospital.

The speaker asked who was to pay for the study.

Dr Lewin answered that Dr Kerr probably believed that the Tuberculosis Association would have something to do with the expense of the study.

A member stated that the Society should approve the general adoption of the study, rather than stipu-

late a trial of approving something that has adequately been proved in other places and thus not contribute anything more than what has been contributed in other places.

Dr Lewin replied that the mention of two hospitals was merely for the purpose of obtaining a report on the experience of those institutions.

Dr Parsons pointed out that some patients routinely admitted to a hospital paid \$10.00 for a chest x-ray film, but that if the State took the x-ray film for \$1.00, the \$10.00 could not be collected.

Dr Biron suggested that, instead of enumerating the number of hospitals, the Society recommend that routine studies be done wherever possible.

The President stated that routine studies should be performed on everybody in the State, and that he believed that the Society should approve in principle universal x-ray studies. He did not, however, believe that the survey should be limited to ordinary patients admitted to general hospitals.

The motion was carried.

Dr Amsden then presented the following report:

Report of the Necrologist

The following members of the New Hampshire Medical Society have died since the last report of the necrologist:

NAME	ADDRESS	DATE OF DEATH
Abbott, Clifton S	Laconia	December 11, 1945
Bates, John H	East Rochester	March 17, 1946
Brown, Lester R	Laconia	November 1, 1945
Cutler, Charles H	Peterboro	December 22, 1945
Foster, George S	Manchester	July 11, 1945
Hildreth, Lewis G	Marlboro	June 25, 1945
Hoyt, Park R	Laconia	August 31, 1945
Joyce, Roland J	Nashua	July 8, 1945
McLaughlin, Patrick J	Nashua	September 8, 1945
Powers, John E	Wilton	July 16, 1945
Sanders, Loren A	Concord	April 24, 1946
Scott, Nathaniel H	Wolfeboro	January 25, 1946
Smith, Henry O	Hudson	May 14, 1945
Tarbell, Wallace H	Contoocook	July 20, 1945
Taylor, Herbert L	Portsmouth	October 24, 1945
Wallace, Ellen A	Concord	November 2, 1945
Wilder, Richard E	Whitefield	August 24, 1945

HENRY H. AMSDEN

Dr Lewin for the Committee on Officers' Reports, moved that the report of the Necrologist be accepted. This motion was duly seconded and was carried.

The speaker expressed the Society's thanks to Dr Lewin and his committee for their excellent work. He then asked whether the delegates approved a request from the New Hampshire Department of Public Welfare for the appointment of Dr John A. Coyle to the Medical Advisory Committee of Ophthalmologists.

The Secretary stated that the Department of Public Welfare had a group of six or seven ophthalmologists with whom they consulted regarding cases of blindness, and that the department selected the men it wished to serve on the committee. As a matter of courtesy, they had always asked the Society to ratify or approve the appointments.

The report of the Committee on Tuberculosis was presented, as follows

Report of the Committee on Tuberculosis

Since the appointment of this committee last May one of its members, Dr Rufus R. Little, formerly superintendent of the New Hampshire State Sanatorium, has accepted the position of superintendent of the Bergen County Hospital at Ridgewood, New Jersey. During his service in New Hampshire Dr. Little made an outstanding contribution to the success of the program for the cure and prevention of tuberculosis. As medical director of the New Hampshire State Sanatorium he greatly expanded the service in chest surgery. This program had been ably inaugurated by his predecessor, the late Dr. Robert M. Deming.

Your committee is happy to report that the State has emerged from World War II without evident injury to the health of its people. The death rate from all causes has decreased to a low point. The tuberculosis death rate, which increased slightly in the year 1943, was reduced to an all-time low—18.7 per 100,000 population—in 1945. This rate is one of the lowest among the states of the Union.

It is an axiom accepted by vital statisticians that the trend in death rates from infectious diseases should be evaluated on the basis of analysis by three-year periods. Study of the tuberculosis mortality statistics on this basis demonstrates that the rate has been maintained on a downward basis for the last thirty years, during which an increasingly intensive campaign has been waged against the disease by the medical profession, public-health workers, the state government and the general public.

Further analysis of the tuberculosis mortality statistics by three-year periods discloses that the reductions in the early years of the intensive attack against the disease were large. As the mortality has declined these reductions have decreased, even with the increasing effectiveness of activities for the eradication of the disease. The average annual tuberculosis death rate for the three-year period 1916-1918 was 117.2 per 100,000 population, and in the succeeding period 1919-1921 was 92.7. This represented an aggregate reduction of 25 per 100,000 population. Again studying the three-year period 1940-1942 we see that the annual average tuberculosis death rate was 26.6. In the three-year period 1943-1945 the rate was 23.3. This is a reduction of 3.3. This analysis demonstrates a well recognized fact, acknowledged by vital statisticians and students of communicable diseases, namely, that it requires even more intensive effort to reduce a low tuberculosis death rate than a high one. The irreducible minimum in the death rate from tuberculosis is conjectural. Some public-health authorities estimate it as a rate of 15 per 100,000 population. If the present effective campaign against the disease is continued we should reach this rate by 1954 (based on an annual average rate for the three-year period at that time). The medical profession, however, has adopted as its goal the virtual eradication of the tubercle bacillus, and will press on to that end.

Many members of the profession and workers in the public-health field feared that the onset of the greatest war in human history would bring about a reversal of the reductions in the tuberculosis mortality. This reversal has not occurred. It may be said that several factors contributed to the continued decline in the death rate during the war years, despite longer hours of labor for the people and the strains and stresses, both physical and mental, under which they worked.

First, the population did not have to undergo serious malnutrition or exposure to debilitating diseases. Second, the medical and public-health resources of the State functioned at a high level of efficiency. These resources were greatly augmented by the tremendous increase in chest x-ray surveys conducted for selective-service registrants in the State Induction Center, in the state-wide program of the New Hampshire Tuberculosis Association in its chest diagnostic clinics and in its schools and college tuberculin-test surveys, and in the joint program of the State Board of Health and the State Tuberculosis Association of chest x-ray films for workers in industry.

During the last five years more than 80,000 chest x-ray films have been taken in these various surveys, in addition

to the large number taken in hospitals throughout the State by request of members of the New Hampshire Medical Society.

So much has been said in this report and in previous reports regarding the encouraging reductions in the tuberculosis death rate that it might be thought that the disease has been brought to a point of minor significance in the lives of the people of the State. This is far from the truth, and such an impression might lead to relaxation of the intensive campaign that has been waged against this disease. Such relaxation of effort would inevitably lead to disastrous results, and the ancient enemy, the tubercle bacillus, would again increase its ravages among the people.

The tragic fact remains that even today tuberculosis is the master thief of human lives and efficiency caused by infectious diseases in the State. The tubercle bacillus is still unconquered and a major cause of disease and death.

In the summer of 1945 one of the members of your committee, aided by the Division of Vital Statistics of the State Board of Health, prepared for general distribution a booklet entitled "Tuberculosis Facts and Figures for New Hampshire," which presented a series of tables and graphs illustrating the status of the tuberculosis problem.

Table VIII in the series is entitled "Tuberculosis—The Leading Cause of Death from Communicable Diseases in New Hampshire for the Past Fifteen Years by Five-Year Periods." The chart portrays the tragic fact that in the five-year period 1940-1944 tuberculosis caused 621 deaths, whereas the following number of deaths were caused by other infectious diseases in the same period: whooping cough, 45; infantile paralysis, 23; measles, 18; scarlet fever, 16; typhoid fever, 7; diphtheria, 2; and smallpox, 2. Nor does this table tell the complete story of the ravages of the disease, which is not one of short duration, but an infectious malady disabling the afflicted for many months and often years whether the outcome is cure or death. The vital statistics tell only of deaths. They do not portray the valiant services of the sanatoriums or the courage and sacrifice on the part of the patients and their physicians and nurses that have resulted in the cure and healing of tuberculosis among thousands of New Hampshire's people.

Two years ago one of the members of your Committee made a study of the diagnoses among persons admitted to the chest diagnostic clinics of the New Hampshire Tuberculosis Association. It was found that the physicians of New Hampshire referred to these clinics for final diagnosis the group of people in whom were discovered the largest number of active cases of pulmonary tuberculosis.

Ten per cent of all patients referred to the clinics that year by the physicians had active cases of pulmonary tuberculosis. One hundred and eighty-five out of the 390 practicing physicians in the State referred patients to the clinic.

There is no doubt that the most important of all case-finding agencies in the fight against tuberculosis in the State are its practicing physicians. It is almost always true that the family physician has the first opportunity not only to ascertain the presence of tuberculosis among the people, but also to give battle for the cure of the afflicted and to safeguard the other members of the family from the tubercle bacillus. For it is to the family physician to whom most people go when troubled by signs of ill health.

The records in the chest diagnosis clinics prove that the physicians of the State, if they are determined to do so, can perform a better job of suspecting and discovering active tuberculosis cases, year in and year out, than any other agency.

In the same study of the population of chest diagnostic clinics it was found that the second largest number of significant cases of tuberculosis was found among the contacts. For the most part these persons were referred to the clinics by the tuberculosis nurses, with the approval of the family physicians.

What of the future? There is no preventive for tuberculosis such as medical science has provided in toxoid for diphtheria and vaccine for smallpox, nor is there any specific cure.

We must carry on and intensify our present program of cure and prevention, utilizing to the fullest extent the resources that have already proved to be so effective.

As has already been outlined in this report, we have arrived at the point of diminishing returns for efforts expended in the tuberculosis program—that is, we must

The Secretary stated that the Blue Shield had no schedule and asked if indemnity payments were wanted. Dr Appleton replied in the affirmative.

This motion was duly seconded and was carried. A member moved that since there was no further business the meeting adjourn. This motion was duly seconded and was carried.

Whereupon, the first meeting of the House of Delegates was adjourned at 11 55 p m

CARLETON R METCALF, *Secretary*

* * *

The House of Delegates reconvened at the Hotel Carpenter, Manchester, on May 14, 1946, at 9 00 a.m., with Speaker Deering G Smith, of Nashua, presiding.

The following members answered the roll call

The President, *ex-officio*
The Vice-President, *ex-officio*
The Secretary-Treasurer, *ex-officio*
Samuel Feiner, Ashland
Earl J Gage, Laconia
Francis J C Dube, Center Ossipee
W J Paul Dye, Wolfeboro
Albert C Johnston, Keene
Marjorie Parsons, Colebrook
Israel A Dinerman, Canaan
Leslie K Sycamore, Hanover
Robert E Biron, Manchester
George C Wilkins (alternate for Samuel Fraser), Manchester
Loren F Richards, Nashua
Robert R Rix, Manchester
Deering G Smith, Nashua
Frank J McQuade, Franklin
William P Clough, Jr, New London
Philip M L Forsberg, Concord
Willard C Montgomery, Epping
Samuel T Ladd, Portsmouth
Robert W Tower, Plaistow
William R Latchaw, Somersworth
Raymond R Perreault, Rochester
B Read Lewin, Claremont

The speaker declared a quorum present

The first order of business was the report of the Nominating Committee by Dr Richards, who nominated for President Drs Ralph W Tuttle, of Wolfeboro, Edward R B McGee, of Berlin, and Charles W Hannaford, of Portsmouth

The Speaker asked if any further nominations for President were forthcoming

Dr Biron moved that the nominations be closed. This motion was duly seconded and was carried.

The Speaker appointed Drs Dinerman, Gage and Feiner as tellers

On written ballot, Dr Ralph W Tuttle was elected president

Dr Richards nominated for Vice-President Drs Clarence Dunbar, of Manchester, Robert Holmes, of Keene, and John Hunter, of Dover

The Speaker asked if there were any additional nominations from the floor

Dr. Biron moved that the nominations be closed. This motion was duly seconded and was carried.

On written ballot, Dr Hunter was elected vice-president.

A partial report of the Committee on Amendments to the Constitution and By-laws was presented by Dr Dye, who stated that the committee moved to amend Section 11 of Chapter VIII of the by-laws to create a new standing committee, to be known as the Council of the New England State Medical Societies, consisting of three members

This motion was duly seconded by Dr Biron

The speaker stated that the title of the committee could not be the Council of the New England Medical Societies

Dr Dye expressed his willingness to have the title changed

The Speaker stated that representatives to the council could be chosen

Dr Sycamore pointed out that the representatives were delegates to the council

Dr Wilkins asked what the former name of the group had been. The President replied that the title was given in old records as "New England Council"

The Speaker stated that the present name was the Council of the New England State Medical Societies and that the council could not be created at the meeting. The members from the Society could be called representatives to the council, delegates to the council or members of the council. He suggested the word "delegates"

The Secretary observed that the title had formerly been the "New England Medical Council" but had been changed to the "Council of the New England State Medical Societies". He preferred to list the delegates as members of a standing committee, as the Committee on Medical Hygiene was listed, with the heading, "Council of the New England State Medical Societies"

The motion, as amended, was carried

Dr Dye moved that Section 11, Chapter VIII, of the by-laws be amended to read as follows

The Committee on the Control of Cancer shall consist of five members whose duty it shall be to study conditions in this state and bring to the attention of the Society and of the general public such matters concerning the prevalence, prevention and cure of the disease as may seem to them advisable

This motion was duly seconded and was carried.

The President then moved that the Secretary cast one ballot for the election of the remainder of the slate of candidates. This motion was duly seconded and was carried

The Secretary announced that he had cast the ballot, electing the officers and committees as named on the slate

The Speaker then declared the officers and committees elected to their respective offices for the ensuing year

Dr Dye, for the Committee on Amendments to the Constitution and By-laws, recommended that the proper section of Chapter VIII of the by-laws be amended to discontinue the Committee on Medical Preparedness, and moved the adoption of this

Dr Biron moved the appointment of Dr J Coyle to the committee. This motion was duly seconded and was carried.

Dr Sycamore stated that he had been instructed by the Grafton County Medical Society to ask that Drs Percy Bartlett and Elmer H Carleton be made life members, and moved that they be made life members. This motion was duly seconded and was carried.

The President read the following letter

Dr Richard W Robiosoo, President
New Hampshire Medical Society
79 Lincoln Street
Lacooia New Hampshire
Dear Dr Robiosoo

March 26, 1946

At two recent meetings, the New Hampshire Roentgen Ray Society, which represents all the radiologists in this state, unanimously reaffirmed that x-ray service to hospitals is a professional, not a hospital service. We are particularly opposed to having diagnostic radiology included as a hospital service in Blue Cross policies, because this creates a discriminatory barrier between the radiologist and the other members of the profession. Radiology requires the services of a medical specialist and therefore represents medical practice. Since hospitals are not permitted to engage in medical practice, they cannot legally sell medical radiologic service to an insurance company. No useful purpose can be served by separating the radiologist from the profession and demoting him to the rank of a nonmedical hospital employee.

We believe that the present situation, if allowed to continue, will result in radiologists' abandoning hospital work and confining their activities to private office practice. This would lower the high standards of hospital service and medical care which the New Hampshire Medical Society and the New Hampshire Roentgen Ray Society attempt to maintain.

Upon request of the New Hampshire Roentgen Ray Society I would, therefore, ask you to give me an opportunity to explain our position to the House of Delegates at the next meeting.

Sincerely yours,

(Signed) FRED S. EVELETH, M.D., President
New Hampshire Roentgen Ray Society

BE IT RESOLVED, That the House of Delegates of the New Hampshire Medical Society hereby expresses itself as opposed in principle to any policy whereby the professional services of any doctor of medicine be charged for and dispensed by any other agent than the doctor concerned, and that the House of Delegates is, therefore, specifically opposed to the present system whereby, in violation of their charters, hospitals dispense for fee the services of roentgenologists and pathologists.

The President added that in the report of Dr Smith, as delegate to the American Medical Association in 1939, as presented to the House of Delegates, it was definitely stated that the American Medical Association had gone on record as taking the same position, and that the only permissible basis on which a hospital could utilize this service was that of a payment of money to a patient, with which the patient could recompense the doctor. He moved the adoption of the resolution. This motion was duly seconded by Dr Clough and others.

Dr Sycamore observed that the directors of the Blue Cross recognize the validity of this position, their only question being whether it was practical, because of the fact that radiologists were in hospitals, and patients considered x-ray study a hospital service. He believed that co-operation among the Blue Shield, the Blue Cross and radiologists would settle the issue.

A member stated that if the proposed change were made, the Enabling Act for selling insurance would result in the transfer of physicians to the Blue Shield from the Blue Cross, since participants of

Blue Cross were not allowed to sell professional services of any description.

Dr Biron recalled that at a recent meeting of the New Hampshire Pathological Society this subject had been discussed in a similar manner and that a similar resolution had been adopted. The Blue Cross contract had also taken up some of the diagnostic work in neurology, in which the situation was analogous to that in the laboratory and the x-ray room, the Blue Cross was considering the matter.

The motion was carried.

Dr Parsons then stated that the welfare patient rates in Coos County should be increased.

A member remarked that he had been approached by the members of a county society regarding the fee of \$20.00, which included prenatal care and delivery and which had not been changed since the war, and that he had been asked to inquire what was being done elsewhere—for example, in the large cities.

The President said that he was sure that the Department of Public Welfare was concerned about the situation and that it would like to meet the proper recompense in welfare cases. Two years previously the fee for office and house calls had been definitely increased, and the department had also permitted the addition of medicine up to a cost of \$1.00, without the necessity of listing the type of medicine given. The President further pointed out that many of the state societies were fumbling through the same problem, the answer to which was a provision for service through insurance, using the basic insurance rate under which patients under the plans could get medical care. The greatest hindrance resulted from the fact that the insurance plan had not been accepted throughout the State. Acceptance was necessary before the Department of Welfare shifted its own medical-care burdens onto the shoulders of physicians.

The Speaker stated that he had been informed by the Secretary that the Department of Public Welfare had increased the rates 25 per cent.

A member inquired whether such a fee included prenatal care. The speaker replied in the affirmative.

A member stated that certain welfare organizations simply referred to a fee schedule made up in the days of the depression by a committee headed by Dr Fuller who took into account the conditions at that time, and that some committee should revise the suggested fee schedule to conform to present conditions.

The President recommended that the Society favor the fee schedule that had become a part of the voluntary insurance plan to cover the care of the indigent of the State.

Dr Appleton moved that a fee schedule for indigent patients be made up by the Department of Public Welfare along the lines of and on the same basis as the Blue Shield.

went up at one point to 60 per cent. The patient, however, grew steadily weaker and had more trouble with burning pain in the buttocks and back, although the burning sensation in the feet disappeared. The appetite began to fail, and he had great difficulty in sleeping because of nervousness and the burning sensation. Weakness became so marked that he confined himself to his room. Some fibrillation in the muscles was noted. Although the patient was afebrile, occasional sweats occurred, and he felt warmer than usual. He was finally admitted to this hospital for study.

Physical examination revealed a nervous, depressed, markedly weakened man, with a flushed face and neck. The thyroid gland was palpable but not enlarged. The heart and lungs were normal. The liver edge was felt four fingerbreadths below the costal margin. The spleen was not palpable. There was an area of hyperesthesia over the left buttock. The legs were somewhat weak, with questionable atrophy about the knees.

The temperature was 98°F, the pulse 120, and the respirations 20. The blood pressure was 130 systolic, 85 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with a hemoglobin of 70 per cent, and a white-cell count of 2500, with 11 per cent segmented and 20 per cent band neutrophils, 3 per cent eosinophils, 42 per cent small lymphocytes, 12 per cent large lymphocytes, 1 per cent immature lymphocytes, 1 per cent monocytes and 5 per cent blast cells of the white series. The red cells varied in size and showed some polychromasia. Several normoblasts and stippled cells were present. The alkaline phosphatase was 14.4 Bodansky units, the serum phosphorus was 4.2 mg, the cholesterol 154 mg, the cholesterol esters 97 mg, the non-protein nitrogen 23 mg and the total protein 6.84 gm per 100 cc, with 4.4 gm of albumin and 2.4 gm of globulin. The van den Bergh test was normal. The bromsulfalein test showed 50 per cent retention of the dye. The prothrombin time was normal. The urine was normal, showing no bile. Several determinations of the basal metabolic rate ranged from +41 to +23 per cent.

X-ray studies of the chest and pelvis were normal. A plain film of the abdomen showed a normal liver and suggestively large spleen.

The patient spent most of his time in bed because of weakness. The pulse ranged between 100 (while the patient was sleeping) and 120. Frequent injections of Demerol were required to relieve the burning pain in the back and buttocks.

On the fifth hospital day a liver biopsy was performed.

DIFFERENTIAL DIAGNOSIS

DR. WYMAN RICHARDSON: Dr. Castleman was good enough to give me a blood smear to examine, which I did before I looked at the record. This blood smear showed abnormal white cells, to which I shall

return, a total white-cell count that was less than normal, with a relative but not absolute increase of lymphocytes, polymorphonuclear neutrophils, what there were of them, showing definite toxic granules, reduced platelets, in conjunction with the decrease in neutrophils, and occasional heavy polychromatophilic and nucleated red cells.

What can one say of such a blood smear? There was red-cell regeneration, as shown by the nucleated red cells and the polychromatophilic cells. What conditions cause such regeneration? Hemolytic anemia might, but hemolytic anemia and reduced platelets do not occur in the same patient. In other words, hemolytic anemias are associated with leukocytosis and an increase of platelets. Red-cell regeneration follows acute blood loss, in which, again, one finds increased platelets. Red-cell regeneration occurs in bone-marrow encroachment. In such cases the white-cell count and the platelets vary, depending on the cause of encroachment. That brings us back to the abnormal white cells. In the record they are given as 5 per cent. The blood smear disclosed 5 per cent or more immature cells, which I could not identify and which may be called stem cells. That percentage seemed high enough to be significant. There were also some necrotic white cells that, if they had been of the same type, would have increased the percentage, there is no way of determining the type.

The blood picture was quite typical of acute leukemia. Do you want me to discuss the case further?

DR. BENJAMIN CASTLEMAN: That is up to you.

DR. RICHARDSON: I shall just run through the protocol.

The reason for extracting the teeth is not indicated in the record.

The chief symptoms in the history were increasing fatigue and a curious type of burning pain over the buttocks and dorsolumbar region that suggests some sort of nerve-root pain.

The description of the blood is consistent with my findings on examination of the blood smear.

I presume that the heterophil reaction was tested in this case in a search for a benign disease. I am not sure whether the barium enema showed diverticulitis or diverticulosis. There is nothing in the record to suggest active inflammatory diverticulitis.

There was no improvement from liver therapy, because the red-cell count was within the limit of error and both the two red-cell counts and the two hemoglobin determinations were comparable, unless done by a photoelectric-cell technic. Therefore, the patient did not respond to treatment on the basis of the evidence given in the record, but he apparently did not lose ground.

Fibrillation in the muscles does not mean a great deal to me. I do not believe that some type of neuromuscular disease need be considered, such a condition occurs with a loss of considerable weight and tissue of any type.

portion of the report This motion was duly seconded and was carried

Dr Dye then asked the delegates to approve a change, which would subsequently be read before the open meeting, in Article IV, Section 1, of the Constitution to read as follows "Section 1 This society shall consist of members, life members and honorary members" He also asked that Article IV, Section 3, be amended to read as follows "Section 3 Life members shall be those members whose dues are remitted"

Dr Biron moved these changes in the Constitution be approved This motion was duly seconded and was carried

Dr Dye moved that Chapter X, Section 1, of the by-laws be amended to read as follows. "An assessment of \$10 00 per capita on the membership of the component societies is hereby made the annual dues of this society"

This motion was duly seconded by Dr Dube and was carried

Dr Sycamore, stating that it was the duty of the House of Delegates to vote in approval of the Board

of Directors of the New Hampshire Physicians' Service, moved that the House approve the following list of directors Harry L Additon, Monsignor Buckley, O E Cain, Francis J C Dube, Fred Fernald, James W Jameson, James M Langley, Joseph E LaRoche, Carleton R Metcalf, J J Morin, Ray W Pert, Richard W Robinson, C A Rollins, James Ross, Frank J Sulloway, Joseph Winter and L K Sycamore

This motion was duly seconded and was carried

The President expressed gratitude to the Manchester Medical Society for their arrangements of this meeting, and moved a vote of thanks

This motion was duly seconded and was carried

The Speaker asked if there were any further business

Dr Biron moved that the meeting be adjourned This motion was duly seconded and was carried

The second and final meeting of the House of Delegates was adjourned at 9 45 a m

CARLETON R METCALF, *Secretary*

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 32391

PRESENTATION OF CASE

A sixty-two-year-old forest consultant entered the hospital because of marked weakness, loss of weight and burning pain over the buttocks and dorsolumbar region

Six months before entry, having previously been in excellent health, the patient noted a sense of fullness in the upper abdomen and put himself on mild dietary restrictions to lose weight Not long after this he noted that he continued to lose weight even though he no longer observed the diet and had a good appetite In the six months before entry he lost 15 pounds Five months before entry he noted excessive fatigue after minor physical exertion and on several occasions felt completely exhausted after an ordinary day's work This fatigability steadily increased until he confined himself to his house and grounds and finally to his room and bed Three months before entry all the

teeth had been extracted A few days later the patient had chills and fever and generalized malaise and felt completely exhausted for ten days A physician discovered that the liver was enlarged, the edge being palpated three fingerbreadths below the costal margin

Examination of the blood at another hospital revealed a red-cell count of 3,900,000, with 12 4 gm of hemoglobin, and a white-cell count of 2350, with 30 per cent neutrophils, 67 per cent lymphocytes, 1 per cent monocytes and 2 per cent eosinophils There was poikilocytosis, anisocytosis and polychromatophilia of the red cells The icteric index was 8 The nonprotein nitrogen was 25 mg, the cholesterol 200 mg, the cholesterol esters 174 mg and the total protein 7 gm per 100 cc, with 4 3 gm of albumin and 2 7 gm of globulin The alkaline phosphatase was 2 5 Bodansky units A heterophil antibody reaction was negative The stools were negative for blood X-ray films of the chest, lumbar spine and pelvis, a gastrointestinal series and an intravenous pyelogram were all reported normal A plain film of the abdomen suggested some enlargement of the liver and spleen A barium enema revealed what appeared to be a mild diverticulitis in the sigmoid area Cystoscopy showed a normal prostate and bladder

The patient complained of a burning sensation in the feet and over the buttocks He was given 2 cc of Lederle's concentrated liver extract twice a week and then once a week, with gradual increase in the red-cell count and hemoglobin to 4,500,000 and 13 gm respectively The white-cell count rose as high as 5600 and the percentage of neutrophils

went up at one point to 60 per cent. The patient, however, grew steadily weaker and had more trouble with burning pain in the buttocks and back, although the burning sensation in the feet disappeared. The appetite began to fail, and he had great difficulty in sleeping because of nervousness and the burning sensation. Weakness became so marked that he confined himself to his room. Some fibrillation in the muscles was noted. Although the patient was afebrile, occasional sweats occurred, and he felt warmer than usual. He was finally admitted to this hospital for study.

Physical examination revealed a nervous, depressed, markedly weakened man, with a flushed face and neck. The thyroid gland was palpable but not enlarged. The heart and lungs were normal. The liver edge was felt four fingerbreadths below the costal margin. The spleen was not palpable. There was an area of hyperesthesia over the left buttock. The legs were somewhat weak, with questionable atrophy about the knees.

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It seems probable that a four-hour chart would have disclosed that the patient actually had fever.

It is always difficult, for me at least, to make an adequate study of sensation, even when involvement of the nerves and nerve roots is known, and it is frequently difficult to demonstrate a definite sensory change. Perhaps the hyperesthesia over the buttock can be regarded as definite evidence of nerve-root irritation, which the history suggests.

I interpret all the laboratory tests, except for the alkaline phosphatase, as normal. The result of the bromsulfalein test suggests involvement of the liver. I assume that the liver and spleen were enlarged. It is difficult to settle this point by x-ray examination, in fact, I am not at all sure that even the pathologist can settle it. I suppose when one weighs any organ one still does not know how much it weighed during life, that is, whether it was heavier or lighter. I can conceive of a spleen that could be shrunken or filled up.

It seems to me that a bone-marrow biopsy was indicated and probably would have given as much if not more information than a liver biopsy.

I have very little to add to my original diagnosis. The blood picture is consistent with that of some disease encroaching on the marrow. The clinical findings suggest anemia and weakness and what appears possibly to have been nerve-root pain. Aside from the findings in the blood, the laboratory tests were essentially negative, except for the increased phosphatase and the bromsulfalein retention. There was possibly an enlarged liver, about which the clinicians and the roentgenologist disagreed to some extent. It seems to me that the clinical diagnosis fitted a subacute or acute — although I should call it subacute — aleukemic leukemia, which is my diagnosis. That means that the liver had presumably been invaded. Invasion of the liver by lymphoma occurs quite frequently, late in the disease, but primary invasion with primary symptoms is unusual. I remember a case with severe changes in which the disease seemed to be largely confined to the liver, with such a rapid downhill course that the patient was believed to have acute degenerative disease of the liver. Such a case is unusual, however, and I should say that the patient in the case under discussion had lymph nodes along the paravertebral areas, with possible involvement inside the spinal canal and with pressure on nerve roots, and that he may also have had a diffuse lymphocytic infiltration of the liver. One might also say that there was no disease of the liver, but the results of the bromsulfalein test remain to be explained. The alkaline phosphatase might be accounted for on the basis of disease involving the bone, with osteoblastic activity, or on the basis of liver disease, most frequently seen in biliary obstruction but perhaps occurring oftener in neoplasm than any other condition. I have found, however, that the alkaline phosphatase is not always dependable. I disregarded it in the last case that I

discussed — much to my discomfiture, because the patient turned out to have malignant tumor with biliary obstruction.

The basal metabolic rate makes one think of thyroid disease. The basal metabolic rate is elevated in both leukemia and aleukemic leukemia. The age of the patient, the way in which the disease progressed and the nerve-root symptoms allow me to make a guess regarding the clinical diagnosis — subacute aleukemic leukemia, probably lymphoblastic. Pathological examination probably disclosed a lymphoblastic lymphoma.

DR LAURENCE L. ROBBINS: This point on the difference of opinion regarding the size of the liver and spleen should be straightened out. I interpreted these films, and although I knew that the liver was enlarged clinically, I could not say that it was enlarged from the films. That is not an infrequent discrepancy. The size of the liver in the x-ray films is not too accurate, whereas demonstration of the size of the spleen is much more accurate. So long as the clinical findings are indicative I should not be disturbed if enlargement of the liver did not appear in the x-ray films.

DR RICHARDSON: The liver is often only two or three fingerbreadths below the costal margin, but no mention is made of the upper level of dullness. Frequently the liver is in a low position and is not enlarged. I believe that four fingerbreadths indicates enlargement, and I accept the statement that the liver was enlarged, there is no statement, however, about the upper limit of dullness.

DR JOHN GRAHAM: The upper limit of dullness, as I remember, was below the fifth rib.

DR RICHARDSON: Then the liver was enlarged.

DR N. M. MARTIN: Should you consider the possibility of a reticulum-cell tumor, as opposed to the lymphoblastic type?

DR RICHARDSON: Yes, only I do not believe that the stem cells or immature cells would have appeared in the blood film.

DR MARTIN: They might, if there had been a large amount of spread.

DR RICHARDSON: In such cases the abnormal cells are monocytes, or an actual monocytic leukemia is present. I cannot tell from this blood picture whether or not the cells were monocytes, which usually occur in patients of middle age.

DR EARLE M. CHAPMAN: Is a low white-cell count and lymphocytosis, in the presence of infiltration in the liver of other cells than monocytic cells, possible in leukemia? Such findings are seen in Chian's disease, in which there are focal areas of liver degeneration.

DR RICHARDSON: There are not usually many abnormal cells in the blood. Any patient with a large congested spleen is likely to have a leukopenia, which is often seen in cirrhosis when there is an enlarged spleen. I should not say that actual liver involvement is necessary.

GRAHAM I saw this patient just a week admission, when the suggestive symptoms weakness, loss of muscular strength and pain-taneous sensations, the most prominent symptom being the severe pain in the back and the burning sensation in the buttocks that kept him awake night, despite every attempt to find a sedative relieve him. The impressive point in the physical examination before admission was the con-ly rapid pulse (120), with a normal tempera-ure. Hyperthyroidism might have been considered, use of a lid lag, a flushed face and neck and a irregular pulse. The patient lay in bed in a house with only a sheet over him, but he ned that he was warmer than anyone else in the se. For over three months he was known to e had an enlarged liver. Smears performed at home failed to reveal any abnormal cells, those e when he first consulted a physician showed a white-cell count, with lymphocytosis. The basal abolic rate was +41 per cent. On admission re was a question of changes in the liver resulting m some form of thyrotoxicosis, cirrhosis, car-oma of the liver or leukemia. Pernicious anemia med to be ruled out when there was no response therapy. I observed the abnormal cells in the ear and inclined toward a diagnosis of leukemia. biopsy was done on the liver rather than the bone ellow chiefly because it was easier and was the e organ that appeared to be pathologically fected.

DR. CHAPMAN Was the patient an alcoholic?

DR. GRAHAM No. He took an occasional drink. it was by no means an alcoholic.

CLINICAL DIAGNOSIS

Aleukemic leukemia

DR. RICHARDSON'S DIAGNOSIS

Subacute aleukemic leukemia (lymphoblastic lymphoma)

ANATOMICAL DIAGNOSIS

Aleukemic leukemia (?monocytic or lymphatic), with massive liver involvement

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN An aspiration biopsy taken by Dr. Wade Volwiler was quite satisfactory. Diffusely infiltrating the liver, more marked in the sinuses, were large abnormal cells that I could not identify with certainty, but that were certainly leukemic cells. I thought that cells of the myeloid series could be ruled out. The cells were typical of either the monocytic or the lymphoid type, I rather favored the former, since many cells had horseshoe-shaped nuclei that were more in keeping with that diagnosis. Dr. Graham showed the slide to Dr. Frederic Parker,

Jr., pathologist at the Boston City Hospital, who was also in favor of the monocytic group.

DR. GRAHAM, will you tell us what happened to the patient after the biopsy?

DR. GRAHAM I cannot give a final answer. It was decided to give some x-ray therapy starting over the back, in the hope of relieving the burning pain in the back if it was due to nerve-root infiltration. After the third or fourth treatment, as I remember it, the patient developed jaundice and became extremely sick, so that the benefit from x-ray therapy was regarded as not worth the attending discomfort. In fact the patient decided that for himself

I should like to ask Dr. Richardson what his experience has been regarding the relation of the basal metabolic level and leukemia. Is there any connection with the white-cell count or any other findings?

DR. RICHARDSON Several people have used the basal metabolic rate as a basis for deciding on the necessity of x-ray treatment. The test is difficult to do accurately. It seems to me that one can get along about as well with one's own clinical findings, such as fever, malaise and the blood picture.

CASE 32392

PRESENTATION OF CASE

First admission A twenty-seven-year-old housewife entered the hospital because of urinary drainage from an operative wound.

The patient's health had been excellent until fifteen months before entry, when she noticed crampy pains in the lower abdomen that began shortly after a menstrual period and gradually increased in severity. She was taken to another hospital, where she was told that she had pelvic trouble and given intensive treatment with penicillin and sulfonamides, to some of which she was sensitive. After a month of this regime a laparotomy revealed bilateral tubal abscesses, with leakage of pus from the left tube. The tips of both ovaries, which were likewise diseased, were resected along with the tubes. Following the operation, the patient noted that when she was given an enema there was leakage from the suprapubic wound, usually consisting of purulent material, but that fecal matter seemed to be extruded when the bowels were loose. Two months before entry a second operation, which was performed to remove the sinus tract, revealed that the bladder was also involved, postoperatively, urine, as well as fecal material, drained from the suprapubic wound. The drainage of urine was particularly profuse when natural voiding was delayed. Although the appetite had returned somewhat, at the time of admission the patient weighed 80 pounds, as compared to her usual 123 pounds. She also had difficulty with postprandial gas and constipation.

Since the onset of her illness she had lost a considerable quantity of hair, and much of what remained had turned gray. The patient had been married five months before she was taken ill. There was nothing in the history to indicate venereal exposure.

Physical examination revealed a poorly nourished woman in no acute discomfort. The heart and lungs were normal. The abdomen showed a palpable nontender mass low in the left lower quadrant. The old midline scar appeared well healed, but along the recent low suprapubic incision there were two draining sinus tracts surrounded by granulation tissue. There was slight clubbing of the fingers and toes.

The temperature was 99.5°F, the pulse 95, and the respirations 20. The blood pressure was 120 systolic, 75 diastolic.

Examination of the blood revealed a hemoglobin of 10.0 gm and a white-cell count of 21,400, with 79 per cent neutrophils and 17 per cent lymphocytes. The total protein was 5.7 gm per 100 cc, with 3.3 gm of albumin and 2.4 gm of globulin. The nonprotein nitrogen was 15 mg, the sugar 90 mg, the calcium 8.8 mg and the phosphorus 4.1 mg per 100 cc. The carbon dioxide was 25.8 milliequiv per liter.

The urine showed a +++ test for albumin, with a few red cells and 250 white cells in clumps per high-power field. Repeated cultures grew colon bacilli and nonhemolytic streptococci.

An intravenous pyelogram revealed slight embarrassment to drainage on the left side but no other abnormality of the upper urinary tract. There was some irregularity of the left side of the bladder, and dye seemed to be escaping, from either the bladder or the left lower ureter, into the surrounding soft tissue and possibly into the bowel. An x-ray film of the chest revealed no evidence of active parenchymal disease, but a few prominent markings in the left first interspace were suggestive of old scars. A barium enema was not entirely satisfactory because of the patient's inability to retain enough barium to fill more than the rectum. The bowel above the level of the sigmoid was widely filled with retained gas and fecal material. At the level of the rectosigmoid, barium escaped into a sinus tract, the destination of which could not be determined.

On the ninth hospital day a transverse colostomy was performed. The patient recovered uneventfully.

Second admission (four months later). The patient showed little or no improvement after discharge. Drainage continued from the sigmoid fistula, producing a thin purulent material rather than feces.

Physical examination and laboratory findings were essentially unchanged from those of the previous admission. On the fifth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. RICHARD CHUTE. This previously healthy woman had been married for five months when she

started to have crampy lower abdominal pains beginning shortly after a catamenial period and increasing in severity so that she was taken to hospital where she was given a month's treatment with penicillin and sulfonamides, apparently with no improvement, since she had to be operated on. At operation bilateral tubal abscesses were present, with leakage of pus from the left tube. The tips of both ovaries were also diseased and were resected along with the tubes.

Although tuberculosis is the cause of only 1 per cent of all cases of salpingitis, that disease seems likely in this case, since the process was acute, with pus draining from at least one tube, even after a month's intensive treatment with penicillin and sulfonamides. This treatment would have been enough to improve greatly any salpingitis due to the gonococcus and would probably have made operation unnecessary. Also, there was nothing in the history to indicate venereal exposure. Other evidence of tuberculosis is that x-ray examination of the chest revealed old healed tuberculosis. Although these x-ray findings were not extensive, there was clubbing of the fingers, suggesting extensive chronic pulmonary disease.

After operation a fistula draining sometimes pus and sometimes feces developed and persisted for more than a year. The fact that it persisted so long without healing suggests that it was due to a chronic disease with little tendency to heal, to a partial obstruction of the intestine distal to the fistula or to the intermittent filling up and spontaneous drainage of an abscess connecting with the bowel, such as might occur with diverticulitis of the sigmoid. The patient was rather young for diverticulitis, but tuberculosis could well account for this condition. If the tubes and ovaries were tuberculous and one tube was leaking frank pus, a tuberculous peritonitis with bowels matted with dense adhesions may have occurred. In such a situation a fecal fistula could easily have been caused accidentally during surgery, or a tuberculous lymph node may have broken down, with abscess formation and a fecal fistula that was kept open by partial blockage of the intestine by a tuberculous peritonitis. Nothing is said about sulfur granules to suggest actinomycosis, and I would not expect endometriosis to give this picture, especially starting from a salpingitis.

Two months before entry an operation not only failed to cure the fecal fistula but also created a urinary fistula. The record states that the bladder was involved, but whether by adhesions or by some active disease is not indicated. One can well imagine that the pelvis was a tangled mass of dense adhesions about a purulent fecal draining sinus, with destruction of all normal anatomy, and that a urinary fistula was accidentally created during surgery. The two months' duration of the fistula was rather long for involvement of the bladder, unless some obstruction to urination existed, which is unusual in a

n, or unless tuberculosis of the urinary tract present, which I am inclined to believe was not the case. The urine showed a +++ test for albumin, with a few red cells and many white cells in high-power field, but the source and therefore the significance of the white cells in the urine is in doubt, since it is not stated whether or not this was a catheterized specimen. It is well known that in the voided urine may contain many white cells from the vagina whereas a catheterized specimen from the same person may show no white cells, in the presence of a urinary fistula, some white and a few red cells would probably have been present, even in a catheterized specimen. The red urine cultures showing a mixed infection of colon bacilli and nonhemolytic streptococci are somewhat against urinary tuberculosis, in which the urine frequently gives a negative culture for the ordinary organisms. Furthermore, there was no history of dysuria or frequency, which usually occurs in urinary tuberculosis, and the intravenous pyelograms were normal. Therefore, I am inclined to believe that tuberculosis of the urinary tract did not exist. In contradistinction to bladder fistulas, those arising from the lower ureter often persist for a long time. On the basis of the x-ray film showing irregularity of the left side of the bladder, slight embarrassment to drainage of the left ureter and escape of the dye from the bladder or the left lower ureter into the surrounding soft tissue, and also because of the history that the drainage of urine was abnormally profuse when natural voiding was delayed, I suspect that in the region of the left ureterovesical junction there was an opening not only into the bladder but also into the lower part of the left ureter.

On admission there was evidence of marked weight loss, anemia, a slight fever and a white-cell count elevated to 21,000. I can find nothing in the laboratory studies that does not fit in with this picture of cachexia and infection or that is of any particular significance in the differential diagnosis. The patient was having difficulty with postprandial gas and constipation, which is consistent with the diagnosis of tuberculous peritonitis. A nontender mass was palpable in the left lower quadrant. This, with the loss of weight and anemia, naturally raises the question of cancer. I prefer to explain the patient's clinical findings on the basis of one disease, however, and therefore guess that this mass was inflammatory and tuberculous.

Following the transverse colostomy the fistula, which the history revealed to be in the sigmoid, did not heal in four months. This may well have been due to obstruction distal to the fistula in the sigmoid caused by the tuberculous inflammation and mass. In fact, obstruction in this area was suggested by the x-ray report that the bowel above the level of the sigmoid was widely filled with retained gas and fecal material.

In conclusion, my diagnoses are healed pulmonary tuberculosis, tuberculosis of both fallopian tubes and of both ovaries, tuberculous peritonitis, with fecal fistula of the sigmoid, urinary fistula in the region of the left ureterovesical junction, and nontuberculous cystitis.

CLINICAL DIAGNOSIS

Vesicosigmoidal cutaneous fistula

DR CHUTE'S DIAGNOSES

Tuberculous salpingo-oophoritis, bilateral
Tuberculous peritonitis, with sigmoidal fistula
Urinary fistula left ureterovesical junction
Cystitis, nontuberculous
Pulmonary tuberculosis, healed

ANATOMICAL DIAGNOSES

Tuberculous salpingo-oophoritis
Tuberculous peritonitis, pelvic
Vesicosigmoidal cutaneous fistula

PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN. At operation the surgeon, Dr Robert R Linton, found the bladder, uterus, adnexa, sigmoid, cecum and appendix fairly well matted together. The rest of the abdominal cavity was free from adhesions. There was a large granulating area in the left side of the pelvis that extended from the suprapubic sinus tract through the broad ligament and to the side of the sigmoid, where a fistula was demonstrated. The left tubo-ovarian mass was removed, and the fistula repaired. An abscess containing about 50 cc of pus was encountered in the right broad ligament close to the appendix. The abscess was drained, and the appendix removed. This raised the question whether the whole process had originated in the appendix. A suprapubic tube was inserted into the bladder, and the wound closed.

Microscopic sections of the tubo-ovarian mass and serosa of the appendix showed active tuberculosis. Postoperatively the patient continued to drain a small amount of pus from the suprapubic wound and was transferred to a sanatorium.

DR ROBERT R LINTON. In my opinion this case illustrates one of the tragedies of surgical treatment of pelvic inflammation, as well as the importance of obtaining material for microscopic examination to establish a diagnosis. When I first saw this patient I did not even think of tuberculosis. I must commend Dr Chute on his excellent discussion of this case, which he analyzed almost perfectly. I had assumed that the vesicosigmoidal skin fistula, which had resulted from the two previous operations carried out at another hospital, was due to an error in surgical technic. The purpose of the defunctioning transverse colostomy was, of course, to divert the fecal current so that a definitive type of operation could be carried out in the pelvis after the

inflammation had subsided. The patient did not improve so much as I had hoped following this operation, but it seemed advisable to proceed with an attempt to close the sigmoid and vesical fistulas. At operation on the pelvis I was unable to visualize anything in the gross that suggested tuberculosis, there was so much secondary infection in the inflamed and ulcerating areas that there was nothing diagnostic of tuberculosis. I made what I thought was a satisfactory closure of the sigmoid fistula, but as follow-up barium enema studies showed, there was still a fistulous tract connecting the pelvis with the sigmoid. This may have been due to the fact that my suture line did not stay closed, or possibly there was another fistula that I did not find.

In view of the x-ray evidence of the persistent fistula it was obvious that the transverse colostomy could not be closed at that time. It was considered

advisable to send the patient to a sanatorium to attempt to build up her physical condition and give the tuberculous process a chance to quiet down. It was hoped that at a later date, after the pelvic inflammatory condition had become arrested, it would be possible to close the transverse colostomy. It may be necessary, however, before doing this to do a complete hysterectomy, with removal of the other tube and ovary. Despite the fact that I did not make a diagnosis of tuberculous salpingitis I do not believe that the plan of treatment would have been changed very much if the diagnosis had been made prior to my second operation. Radical removal of the uterus and adnexa would have been an extremely hazardous procedure in view of the marked secondary infection due to the connection of the sigmoid and vesical fistulas with the pelvis.

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ETHER CENTENARY

THE *Journal* has previously commented on this, the year 1946, as marking the close of a century since anesthesia was introduced to the world as a necessary prelude to major surgery, the demonstration having been made at the Massachusetts General Hospital. Elsewhere in this issue may be found a complete program of the centennial exercises. A century of medical history has given its verdict that the distinction of first appreciating the significance of surgical anesthesia is peculiarly the property of the Massachusetts General Hospital, and it is appropriate that the hospital's outstanding tradition should be based on this discovery.

The occasion of the Ether Centenary is a particularly appropriate one, moreover, at which to present the immediate financial needs of the hospital to the public that it has served so well. These needs are four, comprising a fund to provide a building for the Massachusetts General Hospital Institute of Medical Science, the Massachusetts General Hospital Research Fund to implement this institute, the General Fund to provide for the innumerable expenses of the hospital's operation and the McLean Research Fund to enable the Scientific Research Department of McLean Hospital to further its research in the field of brain diseases and their cure.

The following quotation from an address reprinted in the October 14, 1815, issue of the *Columbian Centinel* seems pertinent at this juncture.

It is not intended to solicit donations by private application to individuals. All good citizens who shall read the address will feel it their duty to contribute in proportion to their ability and will require no further solicitation. The public attention is earnestly called to the facts contained in this address.

And who would be left unmoved by the final paragraph of the address?

To the People of the Commonwealth of Massachusetts

Fellow Citizens

Besides the Undersigned are willing to confess, that they are not ambitious of being the guardians of a charity merely nominal, they are satisfied that the sum, affixed by the Legislature as the condition of its grant, is so small, when compared with the wealth of individuals and the greatness of the state, that no plea, arising from "the hardship of the times," "the general embarrassment of affairs" or "claims of other charities," can or ought avail the community. If such a proposal as this fail, it will be in the judgment of the undersigned, decisive of the fate of the establishment. It will then be apparent, that the will is wanting in the public, to patronize such an undertaking, and that the honor of laying the foundation of a fabric of charity, so noble and majestic, must be left for times, when a higher cast of character predominates, and to a more enlightened and sympathetic race of men.

T. H. Perkins
Josiah Quincy
Daniel Sargent
S. Higginson Jun
Richard Sullivan

Tristram Barnard
George G. Lee
Francis C. Lowell
Joseph May
Joseph Tilden
Gamaliel Bradford

Boston, 8th January, 1814

HOSPITAL SURVEY AND CONSTRUCTION ACT

ORGANIZED medicine will in general welcome the provisions of the Hospital Survey and Construction Act, recently signed by President Truman, as indicated by the support of such organizations as the American Medical Association and the American Hospital Association during the period when the legislation was under consideration in the Senate as the Hill-Burton Bill. For the first time in American history, a balanced and inclusive program providing for a better distribution and an improved quality of hospitals has been established, and this program involves no undue extension of governmental control to private practice.

The act authorizes the appropriation of \$375,000,000 for the construction of hospitals and health centers during the next five years, as well as \$3,000,000 for state-conducted surveys of need. The share of each state in the appropriation for the survey and the construction program will be determined on the basis of population and per-capita income, with the qualification that federal funds may not exceed a third of the total cost of any project. The state must present to the Surgeon General of the United States Public Health Service a plan for construction based on a survey conducted by a single state agency and must appoint a properly qualified advisory council to consult with that agency. Approval of any project depends on sufficient evidence that two thirds of the total cost of construction is available from other than federal sources and that financial support is adequate to maintain and operate the institution after completion. The state is granted latitude to develop and administer its program under standards specified by the Surgeon General and the Federal Hospital Council, which consists of eight members appointed by the Federal Security Administration.

Some of the shortcomings noted by Goldmann¹ in his cogent analysis of the Hill-Burton Bill remain in the act, but there is some question whether these disadvantages are not blessings in disguise. Thus, requirements concerning standards of operation of the hospitals to be constructed are not enumerated, the fees to be charged by participating physicians are not specified, and the amount of the appropria-

tion appears small in view of immediate needs for additions and replacements of hospital buildings. The problem involved is as old as Aesop's King Log: how much — or how little — government is best for the governed. As pointed out in a previous issue of the *Journal*,² the inadequacies of the distribution of medical care are a legitimate concern of government, but the nature of medical standards and the fees to be charged for medical services are matters that are better left to the medical profession, the appropriation, although small in comparison with the billions usually associated with federal grants and agencies, should prove sufficient, when augmented by state funds, to provide for the construction envisaged by the act. These shortcomings offer a challenge and an opportunity to physicians, who by individual and concerted action can render federal definitions, regulations and immense appropriations unnecessary.

REFERENCES

- 1 Goldmann, F. Health bills pending in Congress part three. *New Eng J Med* 234:727-731, 1946.
- 2 Editorial. Inadequacies of medical care. III. Those concerning distribution and cost. *New Eng J Med* 234:539, 1946.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	October 4	Albert H. Brewster
Salem	October 7	Paul W. Hugenberg
Gardner (Worcester subclinic)	October 8	John W. O'Meara
Haverhill	October 9	William T. Green
Brockton	October 10	George W. Van Gorder
Greenfield	October 14	Charles L. Sturdevant
Springfield	October 15	Garry deN. Hough
Worcester	October 18	John W. O'Meara
Pittsfield	October 21	Frank A. Slowick
Hyannis	October 24	Paul L. Norton
Fall River	October 28	David S. Grice

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments.

NOTICES

NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular meeting of the New England Dermatological Society will be held in the Skin Outpatient Department of the Massachusetts General Hospital on Wednesday, October 9, at 2:00 p.m.

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, October 3, in the classroom of the Nurses' Residence at 7:15 p.m. There will be a discussion of unusual post-partum complications. Dr. Bernadette M. Ryder will be chairman.

THE ONE HUNDREDTH ANNIVERSARY OF THE FIRST PUBLIC DEMONSTRATION OF ETHER ANESTHESIA

October 14, 15 and 16 — Massachusetts General Hospital

The Registration Desk will be located in the Rotunda of the Moseley Building at the hospital and all who attend the meetings or the symposiums are requested to register. Information about the various meetings, luncheons and evening functions, as well as tickets, will be obtainable at this desk.

All scientific symposiums will be held at the hospital. The medical public and the general public are cordially invited to attend, no tickets are required, and admission is free.

Those wishing to attend the House-Pupil Alumni Dinner at the Copley-Plaza Hotel should obtain tickets in advance, preferably by mail on the forms that have been sent out for this purpose. These tickets can be picked up at the Registration Desk, and if advance reservations have not been made, reservations and tickets can be obtained at the Registration Desk up to 3:00 p.m. on Monday, October 14. Attendance is limited to house-pupil alumni.

Tickets for the Wives' Dinner held the same night at the Hotel Somerset may also be obtained at the Registration Desk.

Luncheon will be served each day at the hospital for all those attending the symposiums, and on Wednesday, October 16, the luncheon is, in addition, for the house-pupil alumni and their wives.

Applications for tickets to Massachusetts General Hospital Theater Night on Tuesday, October 15, may be reserved by writing to the Ether Centenary Committee at the hospital prior to October 8. These tickets can then be obtained at the Registration Desk. The medical public and all friends of the hospital are cordially invited to this theater performance.

Admission to the Sanders Theater exercises in Cambridge on Wednesday, October 16, at 8:15 p.m. is by invitation only.

A commemorative motion picture of the history of the development of ether anesthesia and methods of manufacture of ether will be shown daily at the hospital and is open to all those attending the meetings.

MONDAY MORNING, OCTOBER 14

9:30 to 12:30

Surgery

DR. EDWARD D. CHURCHILL, *Chairman*

Military Surgery in World War II DR. MICHAEL E. DEBAKEY, New Orleans. Associate professor of surgery, Tulane University of Louisiana School of Medicine.

The Surgical Approach to the Problem of Malignant Disease DR. CHARLES B. HUGGINS, Chicago. Professor of surgery, School of Medicine, University of Chicago.

The Development of Surgery of the Joints DR. MARIUS N. SMITH-PETERSEN, Boston. Formerly, clinical professor of orthopedic surgery, Harvard Medical School, and chief of the Orthopedic Service, Massachusetts General Hospital.

The Present Status of Surgery of the Autonomic Nervous System in Relation to Hypertension DR. REGINALD H. SMITHWICK, Boston. Professor of surgery, Boston University School of Medicine, and surgeon-in-chief, Massachusetts Memorial Hospitals.

MONDAY NOON, OCTOBER 14

Luncheon on the Bulfinch Lawn

MONDAY AFTERNOON, OCTOBER 14

2:00 to 5:00

Progress in the Study of Degenerative Diseases

DR. JOSEPH C. AUB, *Chairman*

The Origin and Nature of Degenerative Joint Diseases DR. WALTER BAUER, Boston. Associate professor of and tutor in medicine, Harvard Medical School, and physician, Massachusetts General Hospital.

Hopeful Aspects of the Future of So-Called Degenerative Cardiovascular Disease DR. PAUL D. WHITE, Boston. Clinical professor of Medicine, Harvard Medical School, and physician, Massachusetts General Hospital.

The Aging of Bone and the Treatment Thereof DR. FULLER ALBRIGHT, Boston. Associate professor of medicine, Harvard Medical School, and physician, Massachusetts General Hospital.

Characteristics of the Mammary Cancer Milk Agent in Mice DR. JOHN J. BITTNER, Minneapolis. George Chase Christian Professor of Cancer Research and director, Division of Cancer Biology, Department of Physiology, University of Minnesota Medical School.

Accelerated and Retarded Aging of the Skin and Its Consequences DR. EDMUND V. COWDREY, St. Louis. Professor of anatomy, Washington University School of Medicine, and director of research, Barnard Free Skin and Cancer Hospital.

* * *

Wives of alumni and of out-of-town guests. Sight-seeing tours (inquire at Registration Desk.)

MONDAY EVENING, OCTOBER 14

6:30

Massachusetts General Hospital House-Pupil Alumni Association Dinner

COPLEY-PLAZA HOTEL

Presiding DR. ARLIE V. BOCK, *President*. Speakers DR. EDWARD D. CHURCHILL, DR. STAFFORD WARREN AND DR. JOHN SNIDER.

Massachusetts General Hospital House-Pupil Alumni Wives' Dinner

HOTEL SOMERSET

TUESDAY MORNING, OCTOBER 15

9:30 to 12:30

The Fundamental Nature of the Anesthesia Process

DR. FRANCIS O. SCHMITT, *Chairman*

The Colloidal Structure of Nerve DR. FRANCIS O. SCHMITT, Boston. Professor of biology, Massachusetts Institute of Technology.

The Effects of Ether and Other Anesthetics on the Electrical Properties of Nerve Fibers and Cells DR R LORENTE DE N6, New York City Member, Rockefeller Institute for Medical Research

The Effects of Narcotics on the Activity and Oxygen Consumption of Nerve DR DETLEV W BRONK, Philadelphia Director, Johnson Foundation for Medical Physics (With Dr F BRINK and Dr P W Davies)

Anesthetics and Cell Metabolism DR RALPH W GERARD, Chicago Professor of physiology, University of Chicago

Correlations and General Remarks DR IRVING LANGMUIR, Schenectady Nobel Laureate and associate director of research, General Electric Company

TUESDAY NOON, OCTOBER 15

Luncheon on the Bulfinch Lawn

TUESDAY AFTERNOON, OCTOBER 15
2 00 to 5 00

Basic Problems of Anesthesia

DR HENRY K BEECHER, *Chairman*

Effect of Anesthetics on Chemical Mediation of Nerve Impulses DR ROBERT D DRIPPS, Philadelphia Assistant professor of surgery (anesthesia), University of Pennsylvania School of Medicine, and director of anesthesia, Hospital of the University of Pennsylvania

The Anesthetic Activity of Fluorinated Hydrocarbons DR BENJAMIN H ROBBINS, Nashville Professor of anesthesia and associate professor of pharmacology, Vanderbilt University School of Medicine

Procaine Block of the Sympathetic Nerves in the Study of Intractable Pain and Circulatory Disorders DR JAMES C WHITE, Boston Assistant professor of and tutor in surgery, Harvard Medical School, and chief of the Neurosurgical Service, Massachusetts General Hospital

Differential Spinal Block DR JULIA ARROWOOD, Boston Instructor in anesthesia, Harvard Medical School, and assistant anesthetist, Massachusetts General Hospital DR STANLEY J SARNOFF, Boston Research fellow in surgery, Harvard Medical School, and clinical fellow in surgery, Massachusetts General Hospital

The Effect of Anesthesia on Cardiac Output in Man DR EVERETT I EVANS, Richmond Associate professor of surgery, Medical College of Virginia (With Dr B W HAYNES and Dr E SMITH)

Some Effects of Anesthesia, Load and Composition on the Excretion of Water and Salt DR CARL A MOYER, Dallas Professor of experimental surgery, Southwestern Medical College (With Dr F A COLLIER, Dr V IOB, Dr L BRYANT and Dr H VAUGHAN)

Implications concerning Cellular Nutrition during Anesthesia DR HENRY K BEECHER, Boston Henry I Dorr Professor of Research in Anesthesia, Harvard Medical School, and chief of the Anesthesia Service, Massachusetts General Hospital (With Dr M F WARREN and Miss A J MURPHY)

* * *

Wives of alumni and of out-of-town guests Music and tea at the Isabella Stewart Gardner Museum (2-00 to 5 00 p m)

TUESDAY EVENING, OCTOBER 15

Massachusetts General Hospital Theater Night

PLYMOUTH THEATER

JOHN C WILSON presents NOEL COWARD and CLIFTON WEBB in "Present Laughter"

WEDNESDAY MORNING, OCTOBER 16

9 30 to 12 30

Physiologic Effects of Wounds

DR TRACY B MALLORY, *Chairman*

The Internal State of the Recently Wounded Man DR HENRY K. BEECHER, Boston

Blood Volume in the Wounded DR FLORINDO A SIMEONZ, Boston Assistant professor of surgery, Harvard Medical School, and assistant surgeon, Massachusetts General Hospital

Blood Chemistry MR SEYMOUR SHAPIRO, Yonkers Director, Biological Laboratory, Arlington Chemical Company

Hematologic Aspects DR EUGENE R SULLIVAN, Boston Assistant in medicine, Massachusetts General Hospital

The Clinical Picture of Renal Insufficiency following Wounding DR CHARLES H BURNETT, Boston Chief resident in medicine, Massachusetts General Hospital

The Pathology of Shock DR TRACY B MALLORY, Boston Assistant professor of pathology, Harvard Medical School, and chief of the Department of Pathology and Bacteriology, Massachusetts General Hospital

WEDNESDAY NOON, OCTOBER 16

Luncheon on the Bulfinch Lawn for Former Massachusetts General Hospital House Pupils and Their Wives

WEDNESDAY AFTERNOON, OCTOBER 16
2 00 to 5 00

The Hospital in the Community

DR J H MEANS, *Chairman*

Ether Day A study in public relations DR REGINALD FITZ, Boston Lecturer on the history of medicine and assistant to the dean, Harvard Medical School, and consulting physician, Peter Bent Brigham Hospital

The Voluntary Hospital — How Can It Survive in the Modern World? DR NATHANIEL W FAXON, Boston Director, Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary

Role of Patients in the History of the Massachusetts General Hospital Miss IDA M CANNON, Boston Formerly, chief of social service, Massachusetts General Hospital

The Hospital A look ahead DR GEORGE R MINOT, Boston Nobel Laureate, professor of medicine, Harvard Medical School, and head of the Harvard Department of Medicine, Boston City Hospital

The Problem of Social Medicine Equilibrating the distribution and technology of medical care MR. WINSLOW CARLTON, New York City Chairman of the Board of Group Health Insurance, Incorporated, New York City

The Teaching Hospital Service to the Public DR ALLAN M BUTLER, Boston Professor of pediatrics, Harvard Medical School, and chief of the Children's Medical Service, Massachusetts General Hospital

5 00

Unveiling of the Daniel Fiske Jones Memorial (Moseley Auditorium)

WEDNESDAY EVENING, OCTOBER 16
8 15

Sanders Theater Exercises, Harvard University (admission by invitation only)

Rt REV HENRY K SHERRILL, *Chairman*

The Need for Wider Research DR RAYMOND B FOSDICK, New York President, Rockefeller Foundation

The Influence of the Discovery of Ether on the Development of Surgery DR EVARTS A GRAHAM, St Louis Bixby Professor of Surgery, Washington University School of Medicine, and surgeon-in-chief, Barnes and St Louis Children's hospitals

The Emergence of Anesthesia's Second Power DR HENRY K BEECHER, Boston Henry I Dorr Professor of Research in Anesthesia, Harvard Medical School, and chief of the Anesthesia Service, Massachusetts General Hospital

Medical Interest in Radioactivity from Becquerel to Bikini DR KARL T COMPTON, Boston President, Massachusetts Institute of Technology

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Volume 235

OCTOBER 3, 1946

Number 14

A THERAPEUTIC SCORE CARD FOR RHEUMATOID ARTHRITIS*

A Standardized Method of Appraising Results of Treatment

OTTO STEINBROCKER, M.D.,† AND ALFRED BLAZER, M.D.‡

NEW YORK CITY

CLINICAL experience and the lack of some accepted system in the literature impressed us with the need for a standardized scheme of appraising therapeutic results in chronic rheumatoid arthritis. We therefore devised the method now used in the Arthritis Clinic of Bellevue Hospital, the so-called "Therapeutic Score Card," which offers an objective and comparatively accurate method of measuring the response to therapy.

One purpose of such a scheme is, so far as possible, to divest therapeutic study of the subjective influence of the patient and of the prejudicial enthusiasm of the physician. Another is to provide a uniform method that can be employed periodically—for example, once a month—on each patient and rapidly enough to be practical and accurately enough to be reliable.

METHOD

The underlying principle of this system is to employ the chief features of rheumatoid arthritis and their response to treatment in determining the effectiveness of any therapeutic agent. To provide an accurate procedure, percentage values are accorded each of the characteristics of the disease, which are tabulated so that exact calculations can be noted and comparisons made.

The scheme is essentially a debit not a credit system. When a patient is first seen all the rheumatoid factors enumerated are noted, and for each one a debit is tabulated. This debit is actually the deduction to be made from a theoretical 100 per cent that represents the status of a recovered or healthy person. If a patient shows inflammatory swelling of the joints, a 50 per cent deduction is entered under the column entitled "Joint Swelling." If the sedimentation rate is elevated, a 15 per cent debit is recorded, and so on down the line of symp-

toms and signs. The patient's debits are then added across the sheet, and the sum deducted from 100. The remainder is scored in the column labeled "Total." Accordingly, a patient first seen may give a balance or total of 35 or 75 per cent, or whatever it may be, signifying a corresponding degree of freedom from rheumatoid disease. In the same fashion at regular intervals, preferably monthly, the therapeutic score is calculated.

As the treatment continues, it is possible by a glance at the record to determine the fluctuations in the patient's rheumatoid status and to discern trends toward improvement or unresponsiveness with an exactness that is calculated and not dependent to any extent on the vagaries of memory, impressions of the patient or the attitude of the observer toward the method of treatment under study. In carrying out therapeutic investigations in this disease, observations are more objective when treatment is prescribed by one person and the calculations made by another, although this method lends itself to reliable estimations by different observers owing to the standard criteria.

At the initial examination it is advisable to note detailed information on all the factors listed. This information serves as the basis of comparison from which all future estimates of progress are derived. The activity of the rheumatoid disease is then assessed and tabulated according to the severity of the features enumerated. After due deliberation we believe that the predominant clinical factors reflecting the activity and progress of rheumatoid disease are joint swelling, sedimentation rate, articular mobility, joint tenderness, weight gain (or loss), hemoglobin (or red-cell count), pain, well-being and functional capacity. Of course the selection of such factors is to some extent a matter of arbitrary decision.

After careful study of our series of rheumatoid patients the criteria were selected and given percentage values determined by much experimental calculation of the factors in the history and course. The features enumerated, we believe, offer a well

*From the Arthritis Clinic, Bellevue Hospital, Fourth Medical Division, New York University.
Presented in summary at a meeting of the New York Rheumatism Association, November 10, 1945.

†Attending physician and chief, Arthritis Clinic, Bellevue Hospital.
‡Assistant clinical professor of medicine, New York University.
§Clinical assistant physician, Bellevue Hospital.

rounded insight into, and evaluation of, the rheumatoid status. As a matter of fact, a difference of opinion regarding the relative importance of several of these items is probably immaterial, so long as specific criteria are chosen and consistently followed throughout in all patients included in a report. The chief principle in the scheme remains that a uniform method of assay is employed and generally accepted, for such a project some criteria must be selected. Obviously the features of rheumatoid disease are not of equal clinical and pathological significance. The relative importance attached to the various characteristics is considered under the discussion of each.

CRITERIA OF IMPROVEMENT

Joint Swelling

Joint swelling is the crucial sign of the rheumatoid process.¹ Unlike tenderness, motion and pain, joint swelling is the most objective index to the patient's progress, of all symptoms, it is also the least affected by emotional influences, voluntary or otherwise. No matter how mild the condition appears or how well the patient seems to be doing, so long as any active inflammation, as evidenced by joint swelling, is present, the patient is suffering from active rheumatoid disease that may flare up at any time or assume a progressive, unfavorable course. For these reasons, before therapy is begun, an initial deduction of 50 per cent for active joint swelling under any circumstances is made. Such a debit makes it impossible for a patient to be classed as recovered or even greatly improved so long as any active articular enlargement persists.

The purpose of these ratings is usually to evaluate the effect of some remedy on the disease. From the therapeutic standpoint, the initial condition is the basis on which the maximum deduction is made.

The amount of swelling is estimated and measured, if possible, at the first examination. The joint most affected is used as the standard. When another joint becomes involved more actively, it becomes the critical one. Regardless of other signs of improvement, any degree of active inflammatory swelling of a joint remains indicative of a persistent rheumatoid process. In the presence of active articular swelling, no matter how slight, no deduction less than 40 per cent is made. Such an allowance indicates that some improvement in the swelling has occurred, but that the continuing inflammatory enlargement remains a serious indication of activity and is as likely to be associated sooner or later with a flare-up as with complete resolution. The importance attached to active joint swelling is a measure of the optimism with which results are regarded — and of their final accuracy. From that attitude, we believe, arise many of the favorable, and ultimately disappointing, opinions on various methods of treatment.

Naturally, the indurated swelling of residual postinflammatory thickening or chronic effusive

synovitis must be differentiated and not given undue significance. Similarly, in elderly patients cardiac or nephritic edema of the ankles and feet should not be mistaken for rheumatoid swelling. The tender lymphedema of the ankles and feet of older rheumatoid patients with varicosities and deep thrombophlebitis, as well as the postural edema of the lower extremities seen in wheel-chair patients and in those who keep their feet over the edge of the bed for long periods, must be recognized.

Erythrocyte Sedimentation Rate

This test is accorded a debit of 15 per cent when sufficiently elevated. The sedimentation rate thereby receives a higher rating than the remaining rheumatoid features. In estimating the significance of the sedimentation rate, we have borne in mind the difference of opinion regarding both the interpretation of a persisting increase in apparently covered patients and the importance of this test compared with joint swelling and other characteristics of the disease. The use of the score card in a series of cases indicates that the sedimentation rate has been given a place proportionate to its clinical role.

Rates of 15 mm by the Cutler method and 75 mm by the Westergren are taken as bases. In other words, if a patient first exhibits an increased rate at or above those points 15 per cent is deducted. In the course of time if the rate goes above the levels, no further deduction is made, because the total debit possible for abnormality of erythrocyte sedimentation is already represented. If the rate falls drops, all or part of the 15 per cent is allowed proportion to the decrease from the original high.

If the record at first shows a sedimentation rate of 75 mm (Westergren method) and a rate of 15 mm at the next determination, 75 per cent is allowed for the improvement so that the score card then registers a deduction of 75 instead of 15 from the original 15 per cent in that column. The score can be scaled according to the same principle for sedimentation rates performed by other techniques.

In the rare cases in which the patient has a normal sedimentation rate to begin with, in the presence of definite clinical signs of rheumatoid activity, a debit is charged for the test. Similarly, when a patient completes treatment and the normal rate remains unchanged, no allowance or deduction is made. In fact, none of the initially normal elements of rheumatoid activity that remain unaltered enter into the calculations. Thus, such signs do not in any way influence the estimate of the patient's response to treatment, which is based on the other abnormal factors manifested. If, on the contrary, a patient appears with a normal sedimentation rate in the presence of other positive signs and finally shows no response to treatment and still presents an elevation of the sedimentation rate at the last examination, the 15 per cent is, of course, charged.

increase the total debit and to show that the patient's condition is worse, at least to the extent indicated by the elevated rate. These are common-se applications of the same principle and are duly acquired by repeated interpretation of the usual picture in these arithmetical terms.

Joint Motion

Joint mobility is given only one twentieth of the significance of the over-all picture — in other words, per cent. Although articular motion occupies an important place in the activities and in the improvement of the patient, the joint inflammation that is usually present so frequently determines articular function that motion is regarded as secondary. At times patients with rheumatoid activity without demonstrable joint swelling suffer some disability. The safer emphasis is considered to be on joint swelling, without completely ignoring joint motion. The improvement of joint mobility, which is rated according to its progress from the original limitation, goes from a debit of 5 per cent to 0 if complete motion is restored, or any part of 5 per cent dependent on the degree of recovery of function.

In severe rheumatoid disease, limited motion or ankylosis is sometimes due to fixed and irreversible changes, such as destruction of cartilage, fibrous or bony ankylosis and subluxation. Naturally, the rheumatoid status should not be discredited because of these conditions. Even if medical treatment is effective, it can only arrest the activity of the disease and cannot improve the irreparable changes and resulting loss of function.

Joint Tenderness

Joint tenderness, like joint mobility, is usually so intimately associated with articular swelling and inflammation in rheumatoid disease that a distinction is almost superfluous. There are patients without definite joint swelling, however, who present joint tenderness as the earliest symptom. There are others in whom the joint swelling has disappeared and whose only evidence of articular involvement is the tenderness elicited by palpation. In such cases slight or great additional features of rheumatoid activity are apparent. So long as the periarticular tenderness persists (especially when compared with palpation of the opposite or other normal or recovered joints), it is best regarded as a sign of continuing activity and given a debit of 5 per cent if unchanged, or any proportion thereof in relation to the initial tenderness. Of course it is essential to distinguish the soreness due to post-rheumatoid periarticular thickening or fibrositis that may no longer signify rheumatoid activity but secondary terminal changes.

Spindle-shaped joints are pathognomonic of rheumatoid arthritis. In some cases, of course, even after the disease is arrested the spindle-shaped deformity persists. The tenderness about such joints

must be carefully evaluated to rule out irreversible periarticular changes as the source of the soreness. If the other signs of rheumatoid activity have resolved, it is safe to assume that in all likelihood the soreness is due to secondary changes. When tenderness continues unduly as a lone symptom, emotional factors must be evaluated. Generalized hyperesthesia should be excluded. Occasionally the previously involved joints become the outlet for psychogenic disorders, complicating the chronic picture and clouding the signs of recovery even after objective signs have disappeared. Pseudoankylosis may be simulated by the same factors, particularly by fear of using joints previously painful on motion.

Hemoglobin

A lowered hemoglobin level is characteristic of most patients with active rheumatoid disease. It becomes, therefore, a fundamental feature of the rheumatoid process. The upper normal value is considered to be 13.5 gm per 100 cc (85 per cent). The hemoglobin is charted at the first examination. If it is above 80 per cent it is considered normal, if it is below 80 per cent, a deduction of 5 per cent is made. If the hemoglobin rises during the course of treatment, a portion of this 5 per cent is reduced according to the degree of improvement toward the normal base. If the hemoglobin remains unchanged at the end of treatment, the same debit is charged, influencing the record of the over-all response of the patient.

Weight Loss

Weight gain is widely accepted as proof of improvement in the patient's general condition when accompanied by other evidence. Avoiding alone is no measure of a satisfactory state, because many patients with active rheumatoid arthritis are overweight. In the usual, asthenic, underweight subject, however, weight gain can well be used as a gauge of response to treatment. In such an underweight patient, provided weight loss has already been noticed during the period of illness, a debit of 5 per cent is made at the outset of treatment. If the patient later shows a gain of more than 1 pound, proportionate credit is given up to recovery of the average weight before illness, which rates a full allowance of 5 per cent.

Pain

Pain represents one of two symptoms included in the score sheet that are purely subjective and in their entirety are given 10 per cent, or one tenth, of the over-all significance of symptoms and signs. Subjective factors are intentionally relegated to a minor place, because they are regarded as the most misleading items in any attempt to arrive at an accurate evaluation of therapy, and are included only because of their widespread use in the literature. To exclude them would probably delay general ac-

ceptance of a standardized method of evaluating therapy. There are enough objective features of rheumatoid disease, as shown in the score card, to guide the assay of any method of treatment without depending too much on the patient's reactions. It is obvious that when joint swelling is improved, joint motion and tenderness ameliorated, relief of pain and a greater sense of well-being almost invariably follow. We have compromised, nevertheless, to the extent that largely subjective responses to treatment are allowed 10 per cent, half of which is allotted to pain.

Even pain can be placed on a more or less objective basis if the patient is initially instructed to take some analgesic, such as aspirin or another salicylate. Some patients are so resigned to their chronic ailment that they prefer to be stoical, in such cases it is gently but firmly insisted that they take medication in adequate doses for relief of pain. In that way, the number of salicylate tablets required daily in the course of time serves as a somewhat objective estimate of the intensity of pain. The initial 5 per cent debit can be scaled down in proportion to the lessening of pain. Loss of sleep due to pain also throws a revealing light on its severity if insomnia is eliminated, at least half the original debit is canceled. The patient's emotional make-up is important in the evaluation of subjective factors, and the examiner must be guided accordingly. The trend of pain response over a period must be taken, and the transient influence of weather and humidity discounted.

Well-Being

The well-being of the patient, which represents an estimate of general subjective response to treatment, includes such factors as mental attitude, loss of anxiety, cheerfulness, confidence, desire to return to some or all of the previous duties and renewed interest in various social activities. Also included are a variety of minor symptoms, which are more or less dependent on some of the features already described and are mentioned merely to outline the scope of this symptom, such as increased appetite, reduced or absent sensations of chilliness and vasomotor disturbance. The interpretation of this phase of the clinical picture depends greatly on the sound judgment of the observer. It is so lacking in objectivity and so reliant on many intangible factors in one way or another that it is allowed only 5 per cent.

Functional Status

The functional status of the patient, to a variable extent, reflects fluctuations in the rheumatoid condition. When increased function arises directly from resolving articular inflammation, the change is adequately registered by improvement in swelling, tenderness and motion. For that reason only 5 per cent is allowed for this feature.

Functional capacity — use of the joints and ability to perform necessary duties or to work — does not necessarily parallel the degree of rheumatoid activity. Few patients whose rheumatoid process becomes inactive fail to acquire greatly enhanced function, unless severe and irreversible joint changes have occurred. Frequently, however, patients under treatment show increased joint function and capacity for work with little or no improvement in the chronic joint inflammation. In fact, some patients with severe rheumatoid polyarthritis continue to work despite pathologic changes and disability far greater than those of others who are incapacitated. The personal equation and many socioeconomic and psychologic factors determine these contradictory manifestations.

The ideal in the therapy of rheumatoid disease would be achieved by the complete arrest of pathologic activity and the physical, economic and social rehabilitation of the patient. Such a goal would often embrace two separate problems: the arrest of rheumatoid activity and the restoration of function or work capacity. The real effect of a specific therapeutic agent must be judged by its influence on the rheumatoid process. The increase of functional capacity cannot be attributed entirely to such a remedy unless the signs of rheumatoid activity are proportionately improved or abolished. This distinction is often overlooked in evaluating the results of a drug.

The enthusiastic atmosphere surrounding the institution of some new method of treatment often temporarily stimulates functional capacity without materially influencing the pathognomonic features of the disease. Increased locomotion effected by any means is naturally welcome but is not retained unless the underlying inflammation has simultaneously been suppressed. Functional capacity usually represents the effect of the whole therapeutic program, including many helpful measures not directly influencing rheumatoid activity, such as physical and occupational therapy, orthopedic aids, analgesics, and the psychologic forces, especially the patient-physician relation. In judging the result of any specific treatment or adjunct, one should therefore regard increased function as subsidiary to the progress of the characteristic signs, as in the score card.

Classification of Response

The chief purpose of the therapeutic score card is to arrive at total values that determine whether the patient is to be classified as apparently arrested, greatly improved, slightly improved or unimproved (or worse). After the patients are classified according to their scores, the results of scoring in each case are compared with an estimate previously made from knowledge of the patient and from the progress notes. From this comparison categories of response can be classified reliably according to the percentage

de on the score card The disease is apparently ested when the score totals 76 per cent or more, otal of 51 to 75 per cent indicates great improve- nt, 26 to 50 per cent slight improvement, and s than 25 per cent no improvement

Table 1 presents the score cards of 4 cases of umatoid arthritis, which are briefly described low The salient features of each case are easily

rheumatoid arthritis for 13 years On November 23, 1943, physical examination at the start of gold therapy revealed swelling of both wrists and the metacarpophalangeal and interphalangeal joints Both knees and ankles were involved, with much periarticular swelling, and there was limitation of joint motion, as well as tenderness and pain on motion A flexion deformity of the right hip joint was noted The erythrocyte sedimentation rate was 20 mm (Cutler method), and the hemoglobin 13.1 gm The patient weighed only 102 pounds and complained of severe pain and pain insomnia She was depressed and felt weak Her functional capacity

TABLE 1 *Therapeutic Score Cards of 4 Patients with Rheumatoid Arthritis*

Case No.	Date	DEBITS					WEIGHT	PAIN	WELL-BEING	FUNCTIONAL CAPACITY	TOTAL (100 MINUS DEBITS)
		JOINT SWELLING	JOINT MOTION	JOINT TENDERNESS	ERYTHROCYTE SEDI-MENTATION RATE	HEMOGLOBIN					
		%	%	%	%	%	%	%	%	%	%
1	11/23/43	50	5	5	0	0	0	5	5	5	25
	8/18/45	0	0	0	0	0	0	0	0	0	100
2	11/23/43	50	5	5	15	0	5	5	5	5	5
	8/3/45	40	0	0	0	0	0	0	0	0	60
3	11/23/43	50	5	5	15	0	5	5	5	5	5
	8/18/45	40	3	3	15	0	0	3	3	3	30
4	10/13/43	50	5	5	15	0	0	5	5	5	10
	8/25/45	45	5	5	15	0	0	5	5	5	15

noted by reference to the score card Patients representing each type of response are included to illustrate their classification in the various categories

CASE 1 (score-card status arrested) P H., a 52-year-old man, was seen with slowly progressing early rheumatoid arthritis of 8 months' duration On November 23, 1943, at the beginning of gold therapy, physical examination showed moderate swelling of the metacarpophalangeal joints of both hands, stiffness and tenderness at these joints and limitation of joint motion Cystic tendonitis, with tenderness, was also noted The average weight was 180 pounds, and there had been no weight loss There was a subjective complaint of moderate pain The patient was uncomfortable but stoical, he had been unable to work for the last 8 months The erythrocyte sedimentation rate was 8 mm (Cutler method), and the hemoglobin 90 per cent Gold therapy was completed on July 15, 1944

Examination on August 18, 1945 revealed no joint swelling, full joint motion and no pain or tenderness There was no change in weight, and full functional capacity was indicated by the fact that the patient had returned to work at his previous job The erythrocyte sedimentation rate was 7 mm (Cutler method), and the hemoglobin was 90 per cent.

CASE 2 (score-card status greatly improved) C C., a 49-year-old woman, had had active, moderately advanced rheumatoid arthritis with a fluctuant course for 12 years On November 23, 1943, at the beginning of gold therapy physical examination disclosed swelling of both wrists and metacarpophalangeal joints and of both knees There were limitation of joint motion and tenderness and severe pain on motion The patient who weighed 114 pounds, had lost weight, and her general physical condition was poor She was able to do only light housework The erythrocyte sedimentation rate was 23 mm (Cutler method), and the hemoglobin was 13.8 gm Gold therapy was completed on January 13, 1945

On August 3, 1945, joint swelling had decreased but slight swelling was present There was no limitation of joint motion or tenderness The erythrocyte sedimentation rate was 12 mm (Cutler method), and the hemoglobin was 14 gm The weight was 128 pounds The patient's general physical condition was excellent, and she was able to do full work

CASE 3 (score-card status slightly improved) C S., a 34-year-old woman, had had ambulatory, active, advanced

was limited to self-care Gold therapy was completed on January 13, 1945

On August 18, 1945, inflammatory joint swelling had decreased but was still present Joint motion had improved about 40 per cent, and joint tenderness had decreased about 40 per cent The erythrocyte sedimentation rate was 23 mm (Cutler method), and the hemoglobin 13.3 gm The patient had gained 28 pounds The pain was less severe, and she was able to sleep with less aspirin Her general outlook was better and she enjoyed food Functional capacity was limited to light work.

CASE 4 (score-card status unimproved) B H., a 58-year-old woman, had had active, early rheumatoid arthritis for 3 months On October 13, 1943, at the start of gold therapy, physical examination showed swelling of both wrists and metacarpophalangeal joints and swelling of both knees and ankles There was limitation of joint motion, as well as tenderness and pain on motion There had been no weight loss, the average weight being 152 pounds Pain was severe, with pain insomnia Her general physical condition was poor, and functional capacity was limited to light housework The erythrocyte sedimentation rate was 25 mm (Cutler method), and the hemoglobin 85 per cent Gold therapy was completed on October 28, 1944

On August 25, 1945 swelling of both wrists and metacarpophalangeal joints had decreased, as had the swelling of both knees There was no swelling of the ankles Limitation of joint motion and joint tenderness were unchanged The erythrocyte sedimentation rate was 25 mm (Cutler method), and the hemoglobin 13.5 gm The average weight was still essentially the same, and severe pain, with insomnia, was present General physical condition was still poor, and functional capacity was unchanged

OTHER FEATURES

Some characteristics of rheumatoid arthritis that are important in the diagnosis or progress of the patient have not been included among the features used for estimating response to therapy because they were not sufficiently informative for our purposes, or because they could only supply overlapping evidence already derived from other items in the score card

The signs that are especially typical of acute and subacute rheumatoid arthritis need no discussion, because our subject is chronic rheumatoid arthritis. A low-grade fever and tachycardia, which are sometimes noted in the course of active, chronic rheumatoid arthritis, are so characteristic of a florid rheumatoid process that they are usually accompanied by definite joint swelling as a more important guide to the patient's progress. In themselves these signs are not sufficiently specific for precise evaluation when they arise as prodromal symptoms of a flare-up in an apparently arrested patient. They merely signalize the probability of an impending relapse requiring close observation and treatment. The characteristic joint swelling of some degree ordinarily appears soon enough to serve as the chief guide to the response to treatment.

Muscle atrophy is usually a sign of advanced arthritis, either active or burnt out. The former process, in which muscle wasting and weakness are secondary manifestations of inflammation, disuse and trophic disturbances, is one of the late signs. Shrinking of muscle is often associated with, but does not give positive evidence of, rheumatoid activity, nor does the degree of atrophy parallel the severity of the activity with which it is allied. When the inflammation subsides, muscle wasting is likely to improve, partly or completely as a result of the abolition of pain, spasm and disability. The lag in muscle recovery, however, is apt to take so long after improvement or arrest of rheumatoid activity that it cannot serve as a practical index to therapeutic response.

Subcutaneous nodules, ganglions (tendon cysts), synovial swelling, nodular tendonitis and tenosynovitis are frequent manifestations of rheumatoid activity. They have not been tabulated in a special column, because they are usually associated with joint swelling and constitute a variation, or additional evidence, of soft-tissue inflammation. Such signs represent invasion of extra-articular, juxta-articular or periarticular structures by the rheumatoid process. Occasionally any of these pathologic changes precede definite joint swelling, persist after joint involvement is no longer discernible, or crop up when the clinical features appear to be improving. In many such cases these symptoms must be interpreted as evidence of rheumatoid activity equivalent to joint swelling and charted accordingly.

Roentgenologic changes offer definite aid in the diagnosis and in the grading of rheumatoid arthritis. When activity diminishes or subsides the x-ray pictures of the joints are slow to reflect the improvement in the articular structures for so long a period that they rarely give assistance in the evaluation of

response to therapy that is not adequately provided by clinical signs.

The demonstration of streptococcal agglutinin in the blood serum is regarded as strong evidence of activity.² The facilities for this test are limited to so few observers that it has been omitted from the score card.

There are other clinical findings, such as lymphadenopathy and splenomegaly, to mention only a few, that are not included. They are encountered too infrequently and their relation to the progress of these patients is too indefinite to warrant special consideration.

Of course, no mechanical scheme for rating the response of patients can be altogether perfect. The yardstick expounded recently by Bayles and Hall³ offers an excellent method of accurately assaying therapy. At times cases that completely defy accurate classification are encountered. According to our experience the number is likely to be small and negligible when a standardized method is employed in a large series of patients.

SUMMARY

The therapeutic score card provides a simple method of charting the effects of treatment on the main features of each patient's rheumatoid arthritis. The total progress, if any, can be summarized readily by the changes reflected in the chief characteristics of the clinical picture. This scheme affords a uniform method of assaying by definite standards a patient's initial condition and later course under therapy. The final classification into degrees of response provides a universally understandable and comparable set of criteria.

Reports based on some such method of scoring, even when derived by different observers, furnish a more consistent and easily correlated pool of information for the evaluation of therapeutic agents than is now available. The following benefits would accrue from the use of an accurately tabulated system embodying certain uniform standards and procedures: specific indexes of rheumatoid activity, assessment of the influence of treatment by the effect on such indexes, uniform rating of total results according to a sliding scale described, and use of an identical nomenclature for the various degrees of response.

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CHIARI'S SYNDROME*

Report of a Case

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CHIARI'S syndrome is a rarely observed clinical entity and is seldom diagnosed during life. It was first adequately described by Budd¹ in 1846 but bears the name of Chiari,² who in 1899 reported more completely 3 cases seen in his clinic and collected 7 additional cases. As first described the syndrome was a manifestation of a primary obliterating endophlebitis of the hepatic veins. Other related pathologic processes have subsequently been shown to produce this disease entity.

The symptom complex manifested by this syndrome is not generally known. A search of the literature reveals only about 70 reported cases. Out of 11,979 autopsies at the Stanford Department of Pathology since 1898, only 5 cases were found, an incidence of 0.42 per cent.³ At the Mayo Clinic, from 1910 to 1939, Kelsey and Comfort⁴ found 20 cases. The syndrome occurs in all ages and with equal frequency in both sexes. Over 50 per cent of the cases reported occurred in patients between the ages of twenty and forty-years,⁵⁻⁷ although the range was between seventeen months and seventy years.

The clinical picture of Chiari's syndrome, which is clearly illustrated by the following case report, is of special interest since the diagnosis was made before death.

CASE REPORT

R. B., a 24-year-old Negro, was admitted to Gallinger Municipal Hospital on December 24, 1943, complaining of increasing weakness, faintness and weight loss for the previous 6 months. During the period of his present illness he had consulted several physicians, and numerous nontoxic medications had been prescribed without avail. The patient admitted consuming about a quart of whiskey daily during the preceding 6 months. He had worked as a laborer first in a printing establishment and more recently in a steel mill. The remainder of the history was not remarkable except that he had eaten clay as a child. He denied any knowledge of venereal infection or treatment with any drugs known to him.

On admission the temperature was 100°F, the pulse 100, and respirations 28. The blood pressure was 130/80. In addition, marked pallor, dental caries and generalized lymphadenopathy were noted. The heart was not enlarged, and there were no thrills or shocks. The heart sounds were of good quality, with a regular rhythm, the aortic 2nd sound was greater than the pulmonic. A soft systolic murmur was audible over the precordium, loudest at the apex and not transmitted to the axilla. The lungs and abdomen were normal.

Laboratory studies revealed the presence of a marked normocytic, normochromic anemia, as demonstrated by a red-cell count of 1,500,000, with 3 gm of hemoglobin. The white-cell count was 2500, with 38 per cent lymphocytes, 30 per cent band neutrophils, 27 per cent segmented neutrophils, 4 per

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cent metamyelocytes and 12 per cent mononuclear cells. The platelet count was 146,000, the reticulocytes numbered 5 to 7 per cent. A Kahn test, a blood culture, the blood urea nitrogen, and urinalysis were normal. Twenty per cent sickling was noted in a 24-hour incubated specimen. The icterus index was 5.

The diagnosis was normocytic, normochromic anemia of unknown etiology.

A week after admission the patient manifested a painful swelling of the right leg that subsided during the following 2 weeks. During this time and for the next 2 weeks the temperature ranged between 100 and 103°F, and the pulse between 80 and 110. The physical findings remained essentially the same as on admission. The patient was given whole-blood transfusions, ferrous sulfate, vitamins and symptomatic measures, with improvement in the general condition and blood picture. The red-cell count rose to 2,550,000, with a hemoglobin of 7 gm, and the white-cell count to 5000, with 29 per cent lymphocytes, 2 per cent monocytes, eosinophils and basophils and 14 per cent band and 51 per cent segmented neutrophils. Meanwhile, studies were undertaken to ascertain the cause of the anemia. X-ray films of the chest, gastrointestinal tract, skull and long bones were entirely negative, as were regular and multiple precordial lead electrocardiograms. Examination of the stools for ova, parasites and blood was completely negative. Repeat blood cultures, blood urea nitrogen levels, various agglutination tests, icterus indexes, stool examinations and urinalyses continued to show no abnormality. The Frei skin test was negative. A first-strength tuberculin skin test was positive.

Two months after admission, a septic temperature developed. The patient appeared gravely ill and complained of abdominal pain, with generalized tenderness and distention. After a few days, he developed diarrhea, which showed no unusual bacteriologic findings but resisted all treatment. A week following the onset of these complaints he developed signs of thrombophlebitis of the left lower leg. Edema of the extremity advanced to involve the scrotum and penis and later the right lower leg. In the interim the liver became enlarged, ascites developed, and a distinct abdominal and thoracic venous pattern appeared. The venous pressure was markedly elevated in the lower extremities and normal in the upper extremities. The general condition became worse, examination of the blood revealed an anemia and leukopenia as severe as that on admission. The venous disease was treated symptomatically, and the previously described supportive measures were continued.

Two weeks after the development of thrombophlebitis chest pain, cough and hemoptysis, with no pulmonary signs, appeared. X-ray examination of the chest showed evidence of a small pulmonary infarct of the right upper lobe and thickened pleura at the right base. Other studies were repeated and were still within normal limits. In April, shortly after the pulmonary infarction, the patient began to improve. Examination of the blood showed a red-cell count of 2,800,000, with 8.5 gm of hemoglobin, and a white-cell count of 6200. Liver-function studies, including repeated hippuric acid synthesis, bromsulfalein and cephalin flocculation tests, were normal. Examination revealed evidences of thickened pleura at the right base, hepatomegaly (1 fingerbreadth below the costal margin) and minimal edema of the ankles. The last 2 months of hospitalization were relatively uneventful except for the development of a lymph-node abscess in the right axilla, which was incised and drained, and a bout of sickle-cell crises, with a decrease in the number of cells, a reticulocytosis of 11 per cent, slight jaundice and increased urobilinogen in the urine. These were minor incidents and apparently had no effect on the course. The patient was discharged on May 17, with diagnoses of thrombosis of the inferior vena cava, Chiari's syndrome and normocytic, normochromic anemia of undetermined etiology.

The patient was to be followed as an outpatient. He returned once for a check-up several weeks after discharge. The findings were unchanged. He was readmitted on June 29, 1944, complaining of fatigue, nervousness, weakness, pains in the wrists, fever and symptoms of an acute upper respiratory infection. Examination revealed a temperature of 102°F, a pulse of 110, an icteric tint to the scleras and skin, pallor, generalized lymphadenopathy, retinal hemorrhages, scattered rales in the left base, moderate cardiomegaly, a precordial (Grade I) blowing systolic murmur, hepatomegaly (1 fingerbreadth below the costal margin) and minimal ankle edema. Examination of the blood showed a red-cell count of 660,000, with 3 gm of hemoglobin, and a white-cell count of 3000, with 40 per cent lymphocytes, 6 per cent mononuclear cells and 7 per cent band and 47 per cent segmented neutrophils. Urinalysis and a Kahn test were negative. The patient was given transfusions and other supportive and symptomatic measures, but he continued to decline and died on the 5th hospital day with essentially no change in the findings. The terminal event was characteristic of a pulmonary infarct.

Autopsy Gross examination revealed a yellow tinge to the skin and scleras. Six hundred cubic centimeters of clear straw-colored fluid was present in the chest on the right and 1000 cc on the left, and 800 cc of fluid was found in the peritoneal cavity. In the pericardial sac there was 100 cc of similar fluid.

The liver was 4 cm below the costal margin. There were a few adhesions between the spleen and surrounding tissues. The liver was smooth, congested, swollen and extremely firm. On cut section there were marked congestion and an irregular yellowish area suggesting fatty degeneration. When the hepatic veins were opened partially organized clots, firmly adherent to the vessel wall, were found. On microscopic examination the liver showed tremendous destruction, hemorrhage and congestion. The bile ducts were dilated and filled with bile. There was thrombus formation in many veins, and periductal fibrosis was marked.

The right lung weighed 725 gm, with roughened pleura over the right upper lobe. The right upper lobe showed increased consistence, and a cavity 2 cm in diameter, surrounded by caseous material, was found in the substance of this lobe. A few calcified nodules were found in the right lower lobe, in addition to areas suggesting old infarcts. The left lung weighed 640 gm and showed areas of old and new infarcts in the lower lobe. Microscopic sections of the lungs revealed the alveoli filled with granular debris in which occasional ghostlike outlines of phagocytic cells were seen. Inflammatory cells surrounded the alveoli. Another section showed an organized thrombus, with fibroblastic proliferation in the surrounding tissues.

The heart weighed 380 gm. There appeared to be slight dilatation of the left ventricle. The endocardium was intact. Slight fibrosis and edema were noted on microscopic examination.

The spleen weighed 455 gm. The capsule was smooth and tense, except at the site of adhesions. On section, the pulp was deep pink, with a firm, almost rubbery consistence. There was a blurred appearance to the architecture. A few small, grayish-pink, round areas were present, suggestive of tuberculous nodules. The structural detail was lost in the infarcted area, which was surrounded by a zone of hyperemia, with diffuse reticular fibrosis. The malpighian nodules were less numerous and conglomerate than those usually seen.

The pancreas, gastrointestinal tract, aorta, adrenal glands and the genitourinary system, including the kidneys, prostate and bladder, were normal.

The inferior vena cava was thickened and narrowed. A dense, firm band formed most of the posterolateral wall. There were adherent patches in its upper portion. It was completely blocked about 2.5 cm below the renal vein where there was an organized, grayish-white, firm thrombus. Similar thrombi were found in the femoral veins. The azygos system was markedly dilated.

The anatomic diagnoses were thrombophlebitis of the hepatic veins, thrombosis of the inferior vena cava, lung abscess of the right upper lobe, multiple pulmonary infarcts, pleural and pericardial effusion and splenomegaly.

DISCUSSION

The case presented above is one of the few reported in which the diagnosis of Chiari's syndrome was

made during life. The development of abdominal pain, hepatomegaly, splenomegaly and ascites superimposed on peripheral edema as a result of peripheral thrombophlebitis made the diagnosis likely. This impression was confirmed at autopsy. This is a case of the chronic form of the syndrome in which prolonged survival was possible. The thrombosis was gradual, the occlusion was incomplete, and recanalization sufficient to allow for adequate collateral circulation and the re-establishment of biliary blood flow.

This syndrome may be due to primary disease of the hepatic venous system or secondary to disease in other parts of the body. Originally it was described as a primary endophlebitis of the veins of the liver.⁸ Simple thrombosis of the inferior vena cava above the entrance of the hepatic veins, with or without involvement of these veins, has also been shown to be responsible for this syndrome. Such thrombosis is frequent in the presence of inflammatory changes in the inferior vena cava,⁹⁻¹⁰ although Thompson and Turnbull¹¹ consider the inflammatory changes secondary to the thrombosis. The two processes are often associated and aid in the propagation of one another. It has been postulated that the entrance of the hepatic veins into the inferior vena cava provides a selective site for thrombosis because of the eddy currents formed at the oblique angle at which the hepatic veins empty into the vena cava.¹²⁻¹⁴ Torsion on the hepatic veins by the liver when in the upright position, causing mechanical damage and scar tissue occluding the veins, has been suggested as another mechanism favoring the production of thrombosis in the hepatic veins.¹⁵ Still another theory proposes that the venous thrombosis results from the retardation or even reversal of flow of venous blood at the diaphragmatic opening of the inferior vena cava as a result of increased intrathoracic pressure on inspiration. Several hypotheses favoring a congenital etiology have been advanced. Rosenblatt¹⁶ believed that the etiology could be fibrosis following a fetal interstitial hepatitis occluding the hepatic veins or preventing their union with the inferior vena cava. Moore¹⁷ suggested that there might be a patent ductus venosus that, as a result of some irritant, began to obliterate and extended to involve the hepatic veins. Another possibility is that the intrauterine process of obliterating many of the venae cavae progresses too far.¹⁸ A congenital stricture at the point of junction of the hepatic veins and inferior vena cava has also been suggested.¹⁹

Intrahepatic and extrahepatic causes have been described as causing thrombosis of the hepatic veins. Rolleston and McNee²⁰ believe that the condition is always secondary — it is frequently secondary to disease elsewhere in the body. Alcoholism,¹ syphilis,²¹ pregnancy¹¹ and chronic cough⁶ have been described as predisposing factors. Of the intrahepatic causes, tumors,^{3, 14, 22} cirrhosis,^{4, 18, 23-24}

umas,^{2, 4} hydatid cysts,^{5, 24} abscesses,^{4, 24} hepatitis^{16, 19} and perihepatitis²⁴ have been described. The mechanism responsible for thrombosis of the hepatic veins is thought to be due to pressure or injury to the veins, causing narrowing of the lumen and slowing of the circulation. Schüppel²⁵ was of the opinion that increased coagulability of the blood was necessary before thrombosis occurred. Many extra-hepatic causes have been reported: pancreatic cysts and enlarged peritoneal lymph nodes,²⁴ nonspecific inflammatory masses,²⁴ anomalies,^{6, 12} trauma,^{6, 15} scars,²⁰ acute or chronic constrictive pericarditis,^{11, 13} tumors,^{3, 4, 24} metastatic carcinomatous invasion or thrombosis of the inferior vena cava,^{3, 26} malignant or infectious emboli,²⁰ thrombophlebitis migrans,¹² local⁵ and general infection^{3, 13, 27, 28} and polycythemia rubra vera.^{25, 29-35}

The association of Chiari's syndrome and sickle-cell anemia in the case reported above aroused interest in the relation between the two diseases. A review of the literature failed to disclose a case of Chiari's syndrome secondary to sickle-cell anemia. It is well recognized that thrombotic episodes occur frequently in patients with this type of anemia, particularly while the patient is in a crisis. Although such episodes in this case did not occur during an exacerbation of the sickle-cell anemia, the development of widespread thrombosis in a patient with this disease is highly suggestive.

The clinical features of this syndrome vary, depending on whether the acute or chronic type is involved and on whether the occlusion is partial or complete and whether recanalization occurs. Hess⁶ in 1905 and Thompson and Turnbull¹⁴ in 1912 elaborated on the clinical aspects of the syndrome. The acute form, which results from a sudden obstruction of the outflow of hepatic venous blood, is manifested by abdominal pain, frequently over the liver and radiating to the back and shoulders, as well as by nausea and vomiting. On examination there is abdominal guarding, rapid, tender enlargement of the liver, splenomegaly on occasion and ascites. Sometimes the patient becomes delirious and comatose and finally goes into shock. Death invariably results in one to four weeks, unless the obstruction is incomplete or recanalization occurs. Jacobson and Goodpasture¹⁴ reported a case in which the patient developed sudden swelling of the liver and acidosis superimposed on signs of inferior vena cava obstruction, indicating occlusive involvement of the hepatic veins.

In the chronic form there is either gradual occlusion of the venous drainage of the biliary system or repeated thromboses in small vessels. The patient develops gastrointestinal symptoms consisting usually of indigestion, epigastric pain, nausea and vomiting. There is gradual enlargement of the liver, occasionally splenomegaly, ascites that reaccumulates rapidly and resists diuretics, a venous pattern on the abdomen and thorax, edema of the lower extremities

and, rarely, cyanosis and jaundice. Hoover¹³ reported a case in which findings did not appear until the occlusion was complete. Low-back pain attributed to congestion of the kidney has been reported as a prominent symptom.

It was postulated by Hutchison and Simpson¹³ that the ratio of collateral circulation to circulation lost by obstruction determines the severity of the symptoms and signs experienced by the patient. Collateral circulation occurs more frequently when the obstruction is gradual than otherwise. In the chronic form there is eventual development of delirium and coma as a result of liver failure. Death invariably occurs in six months, or at the most in several years^{23, 36} and is preceded by signs of liver failure, the hepatorenal syndrome³⁷ or renal failure.^{14, 24} Continued life is possible in limited thrombosis, incomplete occlusion, early recanalization or development of adequate collateral circulation. Hutchison and Simpson¹³ reported a case in which the patient lived for twenty-five years with manifestations of this syndrome, dying only as a result of a laparotomy. Other cases with prolonged survival in which autopsies were not done have been described.

Thompson and Turnbull¹⁴ observed that the collateral circulation on the thorax and abdomen developed more frequently in the chronic than in the acute form. Occasionally the liver is found to be small when the syndrome is secondary to cirrhosis. Hydrothorax with ascites has been reported.^{13, 24, 31} Albuminuria,¹² bilirubinuria,¹² bilirubinemia,¹² lowered plasma cholesterol,³⁸⁻⁴¹ absent cholesterol esters²⁴ and elevated blood urea nitrogen²⁴ are some of the abnormal laboratory findings infrequently found.

The syndrome must be differentiated from cirrhosis of the liver, acute hepatitis, thrombosis of the splenic veins, obstruction of the portal veins, constrictive pericarditis and acute pancreatitis. Abdominal pain—especially over the region of the liver—that sometimes radiates to the back and shoulders, enlargement of a smooth-edged liver and spleen, simultaneous rapid accumulation of ascites, resistance to diuretics, development of a collateral circulation and edema of the legs suggest Chiari's syndrome. The relatively short course of the disease, in addition to the absence of a nodular liver, jaundice, macrocytic anemia and spider angiomas, and normal liver-function studies differentiate the syndrome from portal cirrhosis. Peritoneoscopy also distinguishes the congested liver of Chiari's syndrome from the characteristic appearance in cirrhosis. Acute hepatitis is differentiated by the presence of jaundice, which is invariably absent in Chiari's syndrome, without rapidly accumulating ascites and peripheral edema, which are prominent in the cirrhosis.

Splenic-vein thrombosis is manifested by pain in the left upper quadrant, without tender enlargement

of the liver, ascites or peripheral edema. Obstruction of the portal vein is difficult to differentiate, except that there is rapid enlargement of the liver and formation of ascites with a caput medusae and dilatation of the veins of the abdominal wall. Jaundice, edema and anasarca are rare, and the condition is relatively benign, death being due to hemorrhage or intestinal infarction. Liver enlargement, jaundice and ascites are more marked in hepatic-vein than in portal-vein obstruction. In addition, there are usually leukopenia and anemia in Banti's syndrome.

Constrictive pericarditis is differentiated by a small heart, small pulse pressure, increased venous pressure in the upper as well as the lower extremities, paradoxical pulse, recurring ascites and edema of the lower extremities. Fluoroscopic, kymographic and electrocardiographic studies of the heart help to establish the diagnosis.

A primary tumor of the inferior vena cava may simulate the chronic form of Chiari's syndrome. These two conditions can sometimes be distinguished by the fact that the collateral circulation tends to flow caudad in hepatic vein obstruction and cephalad in inferior vena caval obstruction.

Acute pancreatitis is differentiated by the elevation of the serum amylase and lipase, and absence of a rapidly enlarging liver and symptoms of hepatic obstruction. In addition the shock in pancreatitis is usually out of proportion to the abdominal findings.

The onset of symptoms in the acute form of Chiari's syndrome has been mistakenly interpreted as indicating a surgical emergency of the abdomen.

The pathologic changes in the liver in the syndrome depend on whether the hepatic thrombosis is acute or chronic. In the acute variety the liver appears enlarged, smooth, purplish and highly congested. Wedge-shaped areas are seen if there is occlusion of single branches. The changes microscopically resemble an infarct of Zahn. The central veins are distended or thrombosed, the sinusoids are packed with erythrocytes, and a few inflammatory cells are observed. The central portion of the liver lobule is congested with hemorrhage. Later degeneration and necrosis of the liver cells in this area are seen. If the patient recovers, pseudocirrhosis supervenes. The liver is nutmeg in appearance, nodular and granular, with regeneration of cells and connective-tissue hyperplasia as parenchymal replacement. All degrees of congestion, central necrosis, atrophy and fibrosis are seen, with different stages in various parts of the liver. Compensatory hypertrophy of the uninvolved liver cells occurs. The changes in the chronic form resemble those of cardiac cirrhosis. Such changes have been produced experimentally in animals.⁴²⁻⁴⁷ Thrombosis of the hepatic veins produces portal hypertension and its resultant sequelae. Cirrhosis and primary car-

cinoma have been found superimposed in Chiari's syndrome in a significant number of cases. The relation is not understood, but it is suggestive that the presence of Chiari's syndrome predisposes to these lesions.

There are no known methods of treatment. Recovery or death depends on the rapidity of the obstruction of the hepatic venous drainage, the extent of the occlusion and the time required for canalization and the development of adequate circulation. Omentopexy resulted in death shortly after operation in several reported cases. Other operations to improve the circulation also terminated fatally.

SUMMARY

A case of Chiari's syndrome due to an endophlebitis of the hepatic veins complicating peripheral and inferior vena caval thrombophlebitis is reported. The diagnosis was made during life and confirmed at autopsy. The literature is reviewed, and the differential diagnosis of this syndrome is presented.

We are indebted to Dr. Roger Choisser and the members of the Pathology Department for permission to publish the autopsy findings on this case.

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RECURRENT SPONTANEOUS EMPHYSEMA OF THE MEDIASTINUM WITH CONCOMITANT PNEUMOTHORAX*

Report of a Case

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EMPHYSEMA of the mediastinum has several times been reported in the older literature as a finding in patients with chest injuries or at autopsy. Its occurrence, however, as a disease entity with characteristic clinical symptoms and possible spontaneous onset has been shown only recently by several authors, especially Hamman¹ in 1934. Since that time the publication of a number of clinical reports gives the impression that the condition is not extremely rare.²⁻⁴ A feature of clinical importance is the resemblance of some of the symptoms to those of coronary disease or myocardial infarction. The last fact may at the same time explain why the condition was apparently not recognized more frequently in the past.

The following case report serves as an illustration.

A 37-year-old American engineer was seen on December 22, 1942. The previous history was irrelevant except for three episodes of pain in the chest quoted from old records of the hospital, which are not discussed in detail since there was no definite proof that they were of the same nature as the symptoms described below.

On December 21 the patient had a tight feeling in the lower chest all day, which radiated to the left side of his neck. That evening, while he was sitting quietly in a chair, a rhythmic noise, apparently originating in the chest, struck his ear. The character of the noise was comparable to that of "water dropping on a shelf." The noise was loud enough to be noticed by his wife and by a visitor. One of the physicians of the hospital staff who was called stated that he could hear the sounds at 5 or 6 feet away from the patient's chest.

The patient was sent to the hospital the next morning for examination. He was still complaining about a tight feeling in the heart area but was not in acute distress. The pulse was 80 and slightly irregular and the respirations were normal, without dyspnea or cyanosis, the temperature was normal, and the blood pressure 100/70. Percussion of the heart and lungs revealed no abnormality except for an unusual amount of tympany over the heart area. There was a duplication of the 1st sound over all ostia but not with every heart beat. At that time no sounds could be heard except by stethoscope. A few extrasystoles were noted. No abdominal abnormality was observed, and the area of liver dullness was normal. The blood sedimentation rate (Westergren) was 8 mm in 60 minutes, and the white-cell count was normal.

Röntgenologic examination following ingestion of barium suspension in Trendelenburg's and other positions failed to show either a diverticulum of the esophagus or a hernia of abdominal viscera through the esophageal hiatus or other sections of the diaphragm. The patient's complaints subsided in a short time.

He experienced no similar difficulties until May 31, 1943. That night, without any known cause, he again experienced a dull pain in the cardiac and left infraclavicular areas, and he and his wife noticed rhythmic sounds audible at a distance from his chest. He was seen as an ambulatory patient several times, but was finally hospitalized on June 7 because he did not improve.

When examined on June 1 the patient was not in acute distress, but the pain was still present and was worse when he walked. He was not shortwinded. Physical findings were reported normal, except for an increase of voice and breath sounds on the left side.

On June 2 it was found that the 1st heart sound was preceded by a fine clicking sound "like rales", the 2nd sound was loud.

On June 5 the patient reported that he had heard the sounds in the chest again, especially associated with exercise, bending forward or getting up after lying down.

No new physical abnormalities developed during the 1st week after hospitalization. On June 1 examination of the blood showed a red-cell count of 4,020,000, with a hemoglobin of 84 per cent, and a white-cell count of 7550, with

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1 per cent band and 73 per cent segmented neutrophils, 24 per cent lymphocytes and 2 per cent monocytes. The sedimentation rate was 15 mm in 60 minutes, the fasting blood sugar was 97 mg, and the nonprotein nitrogen 27 mg per 100 cc. By June 7, the white-cell count had increased to 12,100, with 7 per cent band and 73 per cent segmented neutrophils and 20 per cent lymphocytes. The sedimentation rate was 15 mm in 60 minutes. Routine stool and urine examination were negative. On June 10, the white-cell count was 11,400 with 76 per cent segmented neutrophils, 21 per cent lymphocytes, and 3 per cent eosinophils.

By June 13 the patient was feeling better. He could still hear the sounds when lying on his left side supporting himself on his arm and fixing his chest in a certain phase between inspiration and expiration. With the stethoscope a peculiar knocking sound could be heard that was not rhythmic but was apparently synchronous with some of the heartbeats although skipping others.

Several x-ray films of the lungs were taken during this period of observation. An anteroposterior film taken on June 1 showed a few areas of calcification about the left hilus and in the right lower lobe, and a scar in the left apex. No evidence of air in the mediastinum could be demonstrated. Films of the chest taken on June 2 in the right oblique position again showed no air in the mediastinum but revealed a small, marginal left-sided pneumothorax.

The patient was discharged from the hospital on June 20, feeling completely normal. X-ray films of the chest in the anteroposterior and right oblique positions taken on January 19, 1945, for the purpose of follow-up failed to show any recent disease.

DISCUSSION

A comparison of the symptoms in the case presented above with those of several cases reported in the literature appears to justify the diagnosis of spontaneous mediastinal emphysema. A summary of the symptomatology in such cases follows.

Pain, which is a predominant feature, may be severe, moderate or, occasionally, entirely absent. In one of the few cases without pain a nocturnal coughing spell was the initial symptom.⁵ The pain is usually located over the precordium, less frequently laterally in the left chest and seldom in the right chest. Radiation seems to occur more frequently to the back or neck than to the left arm.³ The pain is often influenced by the position of the patient, increasing while he is lying on the left side.

True shock, dyspnea and cyanosis are not characteristic symptoms of this condition,³ although Miller⁶ reports dyspnea in his 4 cases. Marked changes of pulse rate and blood pressure are unusual. A slight elevation of the temperature is infrequently reported.

Inspection occasionally shows a decrease of expansion of the left side of the chest. A frequent and important sign is a tympanitic sound over the precordial area on percussion. A concomitant pneumothorax, often too small to cause any physical symptoms, need not be present to produce the condition.

Most characteristic are the auscultatory findings. The heartbeat may be audible without a stethoscope even at a considerable distance from the chest. This is due to the fact that the heart beats against air in the anterior mediastinum.⁷

With the stethoscope the sounds may be of a crunching, bubbling character,—like the noise

caused by the crumpling of cellophane,—“boiler like” or occasionally grating. They are usually systolic. The intensity of the sounds, like the pain, often increases when the patient turns on his left side.

Associated subcutaneous emphysema is an valuable aid in the diagnosis. It may be located in the neck or in the wall of the chest. The frequent concomitant pneumothorax is another way of escape of the air from the mediastinum.

Slight leukocytosis has occasionally been described.

Roentgenologically the air may be demonstrated in the mediastinum, often better in the oblique than in the anteroposterior view. The finding of a pneumothorax is easier and more frequently described than the demonstration of the air in the mediastinum itself. In view of the mechanism of development of this kind of pneumothorax it is likely that a late stage is represented, and that in the case reported above and similar cases the air had already moved from the mediastinum into the pleural cavity at the time of x-ray examination.

The prognosis in adults is apparently good. In the reports cited all patients recovered.

Most authors believe that spontaneous mediastinal emphysema is usually preceded by interstitial emphysema of the lungs. This condition is probably exceedingly frequent.

Small amounts of air in the pulmonary interstitium are probably resorbed. McGuire and Bean¹ make the following statement:

If a large amount of air escapes it may travel along the interstitial bands toward the hilum and enter the mediastinum. A second, and perhaps commoner pathway for the air to follow is to pass outward directly to the pleura along interstitial bands where it causes the formation of a bleb which may rupture and produce an ordinary pneumothorax. The air may go in both directions, producing both results.

Macklin⁹ inflated the bronchial tree of animals in experimental studies until the alveoli ruptured, and noticed that the air was usually transported to the hilus along the perivascular sheaths. Further inflation caused the air to collect in the mediastinum. Finally, the mediastinal wall ruptured and the air escaped into the pleural cavity.

A concomitant pneumothorax occurs frequently in cases of mediastinal emphysema. Macklin believes that it develops in the same way as in his experimental animals. It is remarkable that, so far, such pneumothorax has always been found on the left side.

SUMMARY

A case of recurrent spontaneous emphysema of the mediastinum, with concomitant pneumothorax, is reported, and the mechanism responsible for this condition is discussed.

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UNILATERAL TREMOR OF THE LOWER EXTREMITY*

Its Association with Internal Derangement of the Ipsilateral Knee

LIEUTENANT COLONEL CHARLES J SUTRO, M C, A U S

ON orthopedic examination of 500 soldiers with recent or long-standing post-traumatic lesions of the knee, the existence of a bizarre type of intentional tremor involving the ipsilateral lower extremity was noted in 8. Most of these 500 soldiers had experienced pain in their knees in civilian life. Each of the 8 soldiers in question complained of recurrent swelling and pain of a single knee and weakness of the ipsilateral leg. Three of the 8 were not able actively to extend the affected leg to 180°, and this was first noted from three to ten years prior to entrance into the armed forces. The tremor was encountered when the involved leg was held in an actively extended attitude of 150° or more. Of further interest was the observation that the existence of this tremor was of more value than atrophy of the thigh in predicting the status of work efficiency of the quadriceps apparatus. Furthermore, the finding of a tremor of a single lower extremity as noted in this study suggested the possibility of a psychosomatic disturbance. On this basis, the test for the tremor provided a ready means to detect psychosomatic disorders in patients with derangement of the knees. It was believed that patients with such tremors were not suitable for elective orthopedic procedures without adequate psychiatric study. An investigation based on the examination of these 8 patients is presented.

PROCEDURE

The patient was seated on the examining table or chair in a position to permit active excursion of the lower extremities. The involved leg was actively extended to its maximal degree, while the opposite leg was held in a relaxed attitude at approximately 90° of flexion. When the test gave a positive reaction, a tremor involving the entire affected extremity, with repeated short excursions of the leg in flexion and extension, was noted from thirty to sixty seconds after the leg was extended to its maximal degree. This tremor, which caused a vertical oscillation of the extremity from one hundred to five hundred times a minute, without any pattern or fixed rhythm, lasted

uninterruptedly for ten minutes — the maximum period of observation. The tremor could be terminated quickly by actively or passively flexing the affected leg to an angle of approximately 90°. The height of the vertical oscillation as measured at the toes varied from 2.5 to 7.5 cm. The patients had no voluntary control over the rate or altitude of the tremor. Furthermore, the use of sedatives, such as phenobarbital and amytal in doses of 65 mg, produced no visible effect on the rapidity of the onset, rate or altitude of the oscillation of the leg. When the examiner percussed the flexed knee of the normal leg of the patient, a temporary increase in the rate and height of the tremor of the affected extended leg was noted. When both legs were simultaneously extended, the tremor was present only in the one with the involved knee (Fig 1). Infre-



FIGURE 1 Photograph of the Lower Extremities
Note that the right foot is out of focus because of the tremor

quently a very mild tremor of transitory nature was observed in the opposite uninvolved extended leg or upper extremities. In 4 of the 8 patients, hyperventilation became apparent four or five minutes after the onset of this test and was accompanied by severe pain in the affected limb. These tests for tremor were repeated each month during the period of two to fourteen months' observation.

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TABLE 1 Clinical Findings in 8 Patients with Tremor of the Lower Extremity Associated with Previous Injury to the Knee

CASE NO.	AGE AT ADMISSION	LENGTH OF SERVICE ON AD-MISSION	PERIOD AFTER INITIAL TRAUMA	LOCAL SYMPTOMS FOLLOWING INITIAL TRAUMA	ATROPHY OF QUADRICEPS MUSCLES	MOVEMENTS AT KNEE	PSYCHIATRIC DIAGNOSIS	X-RAY EXAMINATION OF KNEE	OPERATION	DIAGNOSIS	TOTAL PERIOD OF OBSERVATION AND FOLLOW-UP	DISPOSITION OF PATIENT
	yr	mo									mo	
1	25	3	3 yr	Swelling and pain	Mild	5* restriction to complete active and passive extension of leg	Anxiety neurosis	Negative	None	Flexion contracture (cause undetermined)	3	Separated from service
2	18	1	18 mo	Swelling, pain and locking	Extreme	Free	Normal	Negative	None	Fissure of articular cartilage of patella	13	Retained in service
3*	20	20	2 mo	Swelling, pain and locking	Extreme	Free	Anxiety neurosis	Negative	Arthrotomy (fissure of articular femoral cartilage)	Fissure of articular femoral cartilage	16	Separated from service
4	21	1	6 yr	Swelling and pain	None	Free	Normal	Osteochondritis dissecans of femoral condyle	None	Osteochondritis dissecans of femoral condyle	2	Separated from service
5*	24	4	4 mo	Swelling and pain	Extreme	Free	Mild anxiety neurosis	Negative	Arthrotomy (fissure of articular femoral cartilage)	Fissure of articular femoral cartilage	12	Retained in service
6	24	9	4 yr	Swelling and pain	Mild	5* restriction to active extension of leg, passive extension free	Anxiety neurosis	Negative	None	Fissure of articular cartilage of patella	12	Separated from service
7	26	12	4 yr	Swelling and pain	Extreme	5* restriction to complete active and passive extension of leg	Anxiety neurosis	Negative	None	Flexion contracture (cause undetermined)	12	Separated from service
8	35	6	10 yr	Swelling and pain	Mild	5* restriction to complete active and passive extension of leg	Anxiety neurosis	Negative	None	Flexion contracture (cause undetermined)	4	Separated from service

*Knee injury incurred in line of duty

CLINICAL FINDINGS

Table 1 summarizes the clinical findings. A psychiatric examination revealed that 6 of the 8 patients exhibited general evidence of anxiety neurosis.

Only 1, who had had symptoms for ten years, was prior to these examinations that the involved extremity presented a tremor.

For patients with service-incurred injuries to articular cartilage of the femur developed a tremor of the affected limb after arthrotomy of the knee. They also showed definite physical findings frequently observed in states of anxiety. When 1 of these soldiers was placed in a branch of the service for which he expressed a specific preference, an excellent recovery was obtained. The tremor had completely disappeared within a year after the operation, although marked atrophy of the quadriceps muscles persisted. This soldier could only extend the leg of the affected limb against a considerable amount of resistance to the extensor apparatus. The other soldier was treated in the conditioning, orthopedic and psychiatric sections for a period of sixteen months without any amelioration in the status of the tremor of the limb. It was believed that the environment was a predisposing basis for many of his difficulties. He was, therefore, separated from the Army.

In the nonoperative group of 6, all but 1 of the soldiers were separated from the service. In spite of psychiatric, reconditioning and orthopedic treatment, no improvement was obtained either in the mental or in the physical reactions of these 5 soldiers. In the soldier in whom an excellent adjustment was made, re-examination a year later revealed an absence of the tremor of the affected leg, with a persistence of the atrophy of the quadriceps muscles. This soldier is performing regular duty in the armed forces.

DISCUSSION

One gains the impression that the tremor demonstrated in these 8 cases was similar to that noted in hands affected with writer's cramps or fatigue neurosis. In parallel investigations, a similar tremor was temporarily produced in lower extremities that had recently been immobilized in plaster of Paris bandages for three or more months for treatment of a fractured leg. With exercises and training, the tremor disappeared rapidly in the patients who did not present any tendency toward an anxiety state. From the observations made in these studies, it was suspected that a psychosomatic disturbance had considerable influence on the production and extent of duration of this tremor. For that reason arthrotomy, when indicated, was postponed until a complete psychiatric study had been made. Most soldiers with derangement of the knees who had such

tremors were separated from the service without surgical intervention, since it was almost impossible to obtain a complete mental and physical recovery in the military environment. A change to civilian life was therefore suggested as part of the preoperative and postoperative care of such patients.

Undoubtedly the same sequence of events occurs in persons whose knees are injured in industrial or other accidents, and the identical method of handling such cases appears indicated. The tremor must be differentiated from that caused by malingering, Parkinson's disease or Wilson's disease.¹⁻⁹

SUMMARY

In a group of 500 soldiers with lesions affecting the knee, in 8 there was a coarse tremor limited to the ipsilateral lower extremity that was brought out by active extension of the leg. Six of these patients so affected presented evidence of anxiety states. In 2 of the 8 soldiers the tremor developed after arthrotomy of the knee was performed. Only 1 of the 2 made a complete recovery after vocational readjustment. The other was separated from the service because of aggravation of the tremor. In the nonoperative group of 6, only 1 patient made a recovery after vocational readjustment. The other 5 were separated from the service because the environment was considered to have a decided influence on the persistence of the tremor and symptoms.

The finding of such a tremor in association with lesions of the knee suggests the existence of an anxiety neurosis. When noted, especially in connection with an industrial or other accident or in a member of the armed forces, arthrotomy of the knee should be postponed or avoided until complete psychiatric examination and treatment are pursued. Change in environment, such as separation from the service, is recommended as part of the treatment.

Examination to determine the presence or absence of such tremor is suggested as a routine measure in patients with derangement of the knee joint.

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MEDICAL PROGRESS

PRESENT CONCEPTS OF BENIGN BREAST DISEASE*

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ADVANCES in knowledge of factors concerned in mammary development and function have considerably changed concepts of breast disease in human patients. Through information resulting from systematic surveys, histories, examinations and experimental studies, a new approach to the problem has become available. Since it was demonstrated that hormones were involved in the physiologic response of the breast, it became obvious that they might be of major importance in the genesis of diseases of the mammary gland. Thus, a comprehension of the histology and physiology of the gland is essential to a better understanding of factors that are of possible significance in the initiation of benign and malignant breast lesions. Reviews of the endocrine physiology of the breast have appeared elsewhere,¹⁻³ so that the following discussion is limited to the more pertinent studies. It should be pointed out that much of the present knowledge of the breast is based on animal experimentation, such data are of extreme value, but as has previously been pointed out, caution in the interpretation as applied to human material is necessary.⁴ It is the purpose of this paper to evaluate the available information and to indicate present trends of thought regarding breast disease in human beings.

PHYSIOLOGIC CHANGES

The mammary gland must be considered a part of the female reproductive system and, as such, subject to the same stimuli throughout life as the other organs of reproduction. Changes in the breast seem to be directly related to those occurring in the uterus during the various phases of pituitary and ovarian activity and during pregnancy. Using this concept as a basis, one may review with greater clarity the changes at various periods of life.

At Birth

Activity of the mammary ducts in newborn infants of both sexes is frequent. In addition, mammary enlargement (mastitis neonatorum) and secretion (witch's milk) may occur. These changes originate from endocrine stimuli of maternal origin, since cessation of function and regression of the active processes in the breast follow shortly after delivery.

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At Puberty

After birth the breasts are inactive until the appearance of changes leading to puberty. In the female, development of the breast, which usually begins at about the tenth year, is associated with a definite increase in the activity of the gonads.⁴ At first the changes are confined to the ducts and periductal connective tissue, but even before the menarche there is evidence of acinar and lobule formation. Changes may also be noted in the male breast between the ages of twelve and seventeen.⁴ The histologic picture is similar to that observed at the onset of breast growth in the female. These changes usually subside spontaneously in contrast to those in the female, in which mammary development usually continues once the cyclic activity of the menses is established.

In Cyclic Women

There is convincing evidence that cyclic change occurs in the breast that can be correlated with rise and fall in ovarian activity during the menstrual cycle.⁷⁻¹² Whether these changes are purely epithelial, vascular, secretory or combinations of these is a matter of dispute. Such divergencies of opinion are understandable when it is recognized that studies of whole sections of the breast showed that the degree of activity is not similar throughout.¹¹ This has been attributed to the lack of a uniform response to a given stimulus, that is tissue sensitivity and, as pointed out below, may be a determining factor in certain types of breast disease. Moreover, many of the studies were made on small areas of breast tissue removed coincidentally with localized pathologic processes and therefore should not be considered typical of the normal breast. Review of breast tissue removed from patients dying from various causes is subject to the criticism that the structures may have been altered as a result of the primary disease. Thus, it is apparent that no concrete concept of the changes can be complete until whole sections are made from many normal breasts throughout the menstrual cycle. This is a difficult task, but Foote and Stewart¹² have made an excellent attempt to study such changes from material obtained from apparently healthy women who died accidentally. They were able to predict, with a high percentage of success, the stage of the menstrual cycle from a study of the breast tissue. Since cyclic changes in the endometrium are well recognized and the stage of the menstrual cycle can be determined with con-

erable accuracy from the endometrial pattern, they utilized this technic as a control. They further found that the status of the breast — particularly the lobule — in post-mortem material was vastly different from that in surgical specimens.

Complete development of the breast is manifested by the presence of certain static structures (ducts, lobules and acini). Variations of these structures may occur during the menstrual cycle as a result of rhythmic stimulation with the hormones. The breast is prepared each month for pregnancy, since it is subject to the same influence as the uterus.³ Like the uterus it has both a proliferative phase induced by estrogens and a secretory phase effected by progesterin and the anterior lobe of the pituitary gland. A process analogous to menstruation then occurs and is represented by an involutional change and absorption of the secretion if pregnancy does not ensue. It is only by accepting these possibilities that one may have a concise and logical explanation for the hormonal and nervous action on the breast with the resultant changes during catamenia, pregnancy, lactation and the pathologic states described below.

In Pregnancy and Lactation

Changes during pregnancy and lactation are well recognized and are certainly controlled to a large extent by hormonal secretion. The alterations in the breast in the first half of pregnancy are rapid growth of the lobules and epithelial proliferation, in the latter half the acinar epithelium enlarges and secretes and thus causes distention of the acini.² During pregnancy the placenta is probably the main source of stimulation, whereas during lactation the pituitary gland is the likeliest dominant activator of mammary function.

At the Climacteric

At the menopause, when ovarian stimuli recede to a low ebb, the mammary gland exhibits regressive changes. In some cases evidence of activity in the breast is apparent years after the cessation of the menses. Such activity may be caused by continued but lowered secretion of an activating hormone, possibly from the ovary. In other cases, particularly late in life, there may be an almost complete atrophy of the gland.

In summary, it may be stated that mammary development, growth and regressive changes depend on the rise and fall of hormonal stimuli principally from the gonads and the hypophysis. The exact mechanism by which the metamorphosis takes place is not fully understood. Present knowledge, however, allows at least a working hypothesis for the understanding of some of the diseases of the breast described below.

The Nervous System

Evidence exists that the nervous system is involved in some fashion in the physiologic responses

of the breast. Suckling in the virgin rat resulted in mammary development, lactation and inhibition of the estrous cycle.¹⁵ This presumably works reflexly by way of the hypophysis. In women, suckling certainly plays an important role in the maintenance of lactation. Moreover, numerous cases are cited of lactation and breast changes in children, the virgin female and even in the male after stimulation of the nipple alone.¹⁴ Many lesions of the breast are associated with disease in the pelvis that affects the breast not only by disturbance of ovarian function but also by way of the pelvic sympathetic nerves.¹¹ It must be inferred therefore that the nervous system is important for the maintenance of mammary function, but probably in an indirect manner since the elaboration of hormones may be partially initiated by or dependent upon nervous stimuli.

PRECOCIOUS DEVELOPMENT (INFANTILE HYPERTROPHY)

Aside from the changes noted at birth there are numerous cases of premature mammary development in children. These are usually associated with demonstrable lesions, although in some cases the etiology is vague.

Lesions of the third ventricle. Tumors, defects and inflammatory lesions in the region of the third ventricle give rise to true pubertas praecox. The breast changes are merely part of the general picture of developmental and sexual advance. The most probable explanation for the effect is a stimulation of the hypophysis via the hypothalamus and infundibulum. The breasts exhibit ductal development but rarely lobule formation. Ovaries of these patients show marked follicle development and cyst formation, and in 1 case a true corpus luteum was reported suggesting stimulation by the hypophysis.¹⁶ This activity in the ovary probably initiates the secretion of the hormones, which in turn causes growth of the secondary sex organs, including the breast. This thesis is confirmed by assays of the urine of these patients, which usually show increased levels of gonadotropic hormone, estrogens and 17-ketosteroids (androgens).¹⁷

Lesions of the adrenal cortex. In general, neoplasms or hyperplasias of the adrenal cortex in the female child produce masculinization, but there are cases in which the first signs are feminization.¹⁸ Because the adrenal glands are a probable source of estrogens it is possible to explain the early mammary hypertrophy on this basis, especially since excretion studies reveal increased amounts of the hormone.¹⁶ When masculinization and regression of the breast occur they are accompanied by a significant increase in the androgenic output, even though the estrogen levels usually remain elevated. Thus, it is reasonable to assume that this reversal is of androgenic origin and therefore that the androgens

are not responsible for the original breast hypertrophy

Ovarian lesions Among the associated exciting factors of premature mammary development are lesions such as the granulosa-cell tumor and teratoma of the ovary. These lesions, when active, are usually associated with generalized feminization, breast enlargement, uterine bleeding and cornification of the vaginal epithelium. This syndrome must be distinguished from true pubertas praecox. As in the other states, however, the breast changes are probably produced by estrogens elaborated by the tumors, since the cells involved presumably secrete the hormone. Assays of the urine in most cases reveal elevated excretion levels of estrogens, whereas the titers of the other hormones remain normal.¹⁶

Idiopathic breast development In some children premature breast development occurs without known cause. The process may be transient or may persist. Other secondary sex changes are usually normal or only slightly advanced. Histologic examination reveals ductal development, but for the most part assays of the urine for hormones do not reveal any abnormalities. In the syndrome of osteitis fibrosa disseminata, breast enlargement is a part of the associated sexual precocity.¹⁹

Hormone-induced infantile hypertrophy It has been the experience of many that administration of estrogenic hormone to the female child for gonorrheal vaginitis frequently results in mammary growth. There is no question that these changes are due to the hormone, since regression occurs rather rapidly after cessation of treatment.

In summary, the available evidence suggests that premature mammary development is due in large part to hormonal stimulation. Histologically the changes are confined for the most part to the duct system and periductal connective tissue. Thus, they correspond to a state produced by a known stimulus (estrogens) and in this sense represent a physiologic response to premature or excess secretion of the hormones, as a result of endocrine disturbances. Removal of such a stimulus is followed by a rapid regression to the normal state. Of significance is the fact that precocious development of the breast may be an indication of a pathologic state elsewhere, and as such may be a valuable aid in diagnosis.

HYPERTROPHY

Asymmetrical prepubertal hypertrophy At about the age of ten, when normal breast development usually begins, there may be a rapid growth of one breast that is out of proportion to that of the other. This is often referred to as "early ripening" and is not true hypertrophy. Eventually the more slowly developing breast usually attains the size of the larger breast, and at the time of puberty both are of almost equal size and within normal limits. Since

in most females the breasts are not identical in size, this seems to represent an exaggeration of a normal phenomenon. Histologically the changes are no different from those in the normal adolescent. Estrogen excretion is usually normal. The early inequality is explained by some investigators as an increased sensitivity of the involved organ to a normal physiologic stimulus.

Pubertal and postpubertal hypertrophy Pubertal and postpubertal hypertrophic abnormalities may be classed as true hypertrophy. The process is either unilateral or bilateral and is easily distinguished from early ripening by the size of the breast. It may first manifest itself at puberty, although similar changes are associated with pregnancy and lactation. Histologically there is an increase in ductal growth, but connective-tissue increase is more striking. Lobular development is rare especially in the virginal type. Estrogen assays are usually normal but may show elevated levels of the hormone. Again, as in early ripening, the changes may be due to an excessive stimulation or to increased sensitivity of the breast involved.

FIBROADENOMA

Fibroadenomas of the breast are the most frequent tumors in young women, the majority appearing between the second and third decades. The lesions are generally slowly growing and although not noticed may arise in the early years after the menarche when atypical menstrual activity is not unusual. They resemble the changes seen in early ripening and hypertrophy. They are rare before puberty and after the menopause, except possibly in the presence of a granulosa-cell tumor of the ovary. It has been suggested that the greatest incidence of the tumor is in women of a definite constitutional type — nulliparous women with a relative underdevelopment of the pelvic organs and breast.²⁰ Fibroadenomas are also found, however, in association with hypertrophy of the breast in a small percentage of cases. Changes have been observed in the size and histologic appearance of these tumors during the menstrual cycle,¹⁸ pregnancy and lactation.^{21, 22}

Fibroadenomas are distinctly different from other lesions of the breast, in that they may respond to a stimulus in the same fashion as normal breast tissue. It has therefore been suggested that they are not true tumors but merely a localized response to a normal stimulus as a result of a specific tissue sensitivity, such a response is akin to the grosser manifestations of early ripening and asymmetrical hypertrophy. This thesis is enhanced by the fact that the lesions may be multiple and may continue to appear as mammary development progresses. In addition, areas resembling fibroadenomas may be found in a breast without actual formation of a mass. Observation suggests that these lesions are of hormonal origin. It is possible that they arise as a result of abnormal or excessive stimulation, since they usually

when the metabolism and secretion of the sex hormones are at their height and may be abnormal. It is difficult to explain why circulating hormones do not affect the breast tissue in a uniform manner, but as stated above, present evidence suggests that such lack of uniformity exists and probably depends on individual susceptibility.^{10, 23}

CHRONIC CYSTIC MASTITIS

pointed out frequently in the last few years, clinicians and pathologists often use this terminology as a catchall for a variety of benign lesions without tumor formation. It is now recognized that some of the lesions included under the diagnosis of chronic cystic mastitis can be distinguished as distinct entities and should be so designated. I am in accord with this point of view and plead for the term chronic cystic mastitis be discarded. It is essential that a working classification based on clinical and microscopic evidence be established in investigation of possible causative factors and natural history of any specific lesion. A number of writers have attempted to establish such a classification, but because of variations in interpretation of nomenclature, confusion exists even among those who have made special efforts to study the problem, owing partly to the difficulty in observing the process as it develops and partly to the variety of changes that coexist in the same breast. At any rate, the situation is being clarified, and it is likely that agreement among the various workers will be forthcoming as more material is studied and correlated. The importance of unanimity of opinion lies in the fact that some lesions included in the diagnosis of chronic cystic mastitis may lead to cancer, whereas others may be of no significance. Discussions dealing with this subject should be reviewed and evaluated by the interested reader.^{2, 13, 14, 24-30} It is not within the realm of this review to attempt a continuation of apparently contradictory viewpoints. Nevertheless a description of clinical syndromes frequently seen is indicated, to stimulate further investigation and clarification.

A syndrome in which the earlier signs are characterized by premenstrual swelling and pain associated with tenderness on palpation seems to be a distinct entity. The relief following the onset of the menses is dramatic. It is recognized that similar symptoms may be present in apparently normal women and, as has been stressed, may be an integral part of the normal breast cycle in preparation for pregnancy. The patients seen by the physician, however, usually have an aberration of an apparently normal process. The early physical signs are usually minimal and, besides slight premenstrual swelling and venous engorgement, may reveal only a slight thickening in the upper outer quadrant. Histologically there may be only a slight increase in the periacinar connective tissue and edema. As the process continues the symptoms and signs be-

come more prominent. There may be only an accentuation of nodularity in the upper outer quadrant, but usually the process is more extensive. There may be an increase in the density of the breast, which is well differentiated from the overlying skin, the subcutaneous tissue and the underlying structures. In the advanced stages the entire breast resembles a saucer or disk, and a definite edge can be palpated. The gland may be finely granular or nodular and in the premenstruum exhibits marked swelling and venous dilatation that may account for the cyclic pain. On microscopic examination there is usually a marked increase in the connective tissue stroma, with loss of or defective lobule formation. Frequently, in addition, there is proliferation of the acini, although the epithelium itself is not hyperplastic. Many variations of the process are seen. These lesions usually occur in the second and third decades of life in women who have not been pregnant. The process resembles both clinically and histologically the localized fibroadenoma. Menstrual cycles may be of shorter intervals than usual, accompanied by a scant flow of short duration. The incidence of sterility is high, and in women who have borne children the lesion is sometimes seen after a long period of infertility. Terms suggested for such processes are "adenofibrosis,"²⁴ "lobule alteration"¹³ and "fibroadenomatosis."²⁵ The secretions of the ovaries seem to be a prerequisite for the production of this syndrome, although they may not be the exciting factors. Nervous stimuli, vascular reaction and the mechanisms of hormonal secretion are closely interwoven, so that all three factors may be involved in the process, particularly regarding the edema and congestion. Excretion studies are slightly suggestive of a hormonal imbalance. The possible role of unopposed or atypical stimulation by the hormones also remains to be clarified. Slight abnormalities in the menstrual cycle and associated pelvic disease suggest a hormonal etiology. It can be concluded that, as in fibroadenoma, the hormones are involved but that other factors are necessary for the production of the syndrome.

Another lesion is characterized by discharge from the nipple. The process is sometimes associated with swelling and cyclic or acyclic pain. The discharge may abate at the menses, but generally persists throughout the cycle. It may be serous or may resemble colostrum and show varying degrees of viscosity. It is to be distinguished from the serosanguinous or sanguinous discharge frequently associated with duct papillomas, marked epithelial hyperplasias and carcinoma. Examination usually reveals dilatation of the ducts that is sometimes segmental and simulates cysts, especially near the areola. The dilated ducts can usually be palpated as cordlike structures radiating from the nipple. Slight nodularity may be found elsewhere in the breast. The nipples are frequently crusted, the mammary tissue itself is ill defined, and the breast

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cur when the metabolism and secretion of the sex hormones are at their height and may be abnormal as well. It is difficult to explain why circulating hormones do not affect the breast tissue in a uniform manner, but as stated above, present evidence suggests that such lack of uniformity exists and probably depends on individual susceptibility.¹⁰⁻²³

CHRONIC CYSTIC MASTITIS

As pointed out frequently in the last few years, both clinicians and pathologists often use this terminology as a catchall for a variety of benign lesions without tumor formation. It is now recognized that some of the lesions included under the diagnosis of chronic cystic mastitis can be distinguished as definite entities and should be so designated. I am fully in accord with this point of view and plead that the term chronic cystic mastitis be discarded. It is essential that a working classification based on clinical and microscopic evidence be established for an investigation of possible causative factors and a natural history of any specific lesion. A number of writers have attempted to establish such a classification, but because of variations in interpretation of nomenclature, confusion exists even among those who have made special efforts to study the problem, owing partly to the difficulty in observing the process as it develops and partly to the variety of stages that coexist in the same breast. At any rate, the situation is being clarified, and it is likely that agreement among the various workers will be forthcoming as more material is studied and correlated. The importance of unanimity of opinion lies in the fact that some lesions included in the diagnosis of chronic cystic mastitis may lead to cancer, whereas others may be of no significance. Discussions dealing with this subject should be reviewed and evaluated by the interested reader.¹³⁻¹⁴⁻²⁴⁻³⁰ It is not within the realm of this review to attempt a classification of apparently contradictory viewpoints. Nevertheless a description of clinical syndromes frequently seen is indicated, to stimulate further investigation and clarification.

A syndrome in which the earlier signs are characterized by premenstrual swelling and pain associated with tenderness on palpation seems to be a distinct entity. The relief following the onset of the menses is dramatic. It is recognized that similar symptoms may be present in apparently normal women and, as has been stressed, may be an integral part of the normal breast cycle in preparation for pregnancy. The patients seen by the physician, however, usually have an aberration of an apparently normal process. The early physical signs are usually minimal and, besides slight premenstrual swelling and venous engorgement, may reveal only a slight thickening in the upper outer quadrant. Histologically there may be only a slight increase in the periacinar connective tissue and edema. As the process continues the symptoms and signs be-

come more prominent. There may be only an accentuation of nodularity in the upper outer quadrant, but usually the process is more extensive. There may be an increase in the density of the breast, which is well differentiated from the overlying skin, the subcutaneous tissue and the underlying structures. In the advanced stages the entire breast resembles a saucer or disk, and a definite edge can be palpated. The gland may be finely granular or nodular and in the premenstruum exhibits marked swelling and venous dilatation that may account for the cyclic pain. On microscopic examination there is usually a marked increase in the connective stroma, with loss of or defective lobule formation. Frequently, in addition, there is proliferation of the acini, although the epithelium itself is not hyperplastic. Many variations of the process are seen. These lesions usually occur in the second and third decades of life in women who have not been pregnant. The process resembles both clinically and histologically the localized fibroadenoma. Menstrual cycles may be of shorter intervals than usual, accompanied by a scant flow of short duration. The incidence of sterility is high, and in women who have borne children the lesion is sometimes seen after a long period of infertility. Terms suggested for such processes are "adenofibrosis,"²⁴ "lobule alteration"¹³ and "fibroadenomatosis."²⁵ The secretions of the ovaries seem to be a prerequisite for the production of this syndrome, although they may not be the exciting factors. Nervous stimuli, vascular reaction and the mechanisms of hormonal secretion are closely interwoven, so that all three factors may be involved in the process, particularly regarding the edema and congestion. Excretion studies are slightly suggestive of a hormonal unbalance. The possible role of unopposed or atypical stimulation by the hormones also remains to be clarified. Slight abnormalities in the menstrual cycle and associated pelvic disease suggest a hormonal etiology. It can be concluded that, as in fibroadenoma, the hormones are involved but that other factors are necessary for the production of the syndrome.

Another lesion is characterized by discharge from the nipple. The process is sometimes associated with swelling and cyclic or acyclic pain. The discharge may abate at the menses, but generally persists throughout the cycle. It may be serous or may resemble colostrum and show varying degrees of viscosity. It is to be distinguished from the serosanguinous or sanguinous discharge frequently associated with duct papillomas, marked epithelial hyperplasias and carcinoma. Examination usually reveals dilatation of the ducts that is sometimes segmental and simulates cysts, especially near the areola. The dilated ducts can usually be palpated as cordlike structures radiating from the nipple. Slight nodularity may be found elsewhere in the breast. The nipples are frequently crusted, the mammary tissue itself is ill defined, and the breast

is lax. If secretion is not obvious, removal of the crust, with gentle pressure on the breast, usually results in the escape of fluid from the nipple. On gross and microscopic examination the ducts are dilated and contain secretion, desquamated cells and debris. Cheesy, inspissated material and segmental dilatations, which appear cystic, are often seen. Hyperplasia of the duct and acinar epithelium may be superimposed. A sequel of duct stasis and dilatation may be erosion of the epithelial lining.¹³ If the surrounding stroma is fatty, a reaction as manifested by fat necrosis may be seen. These lesions occur most frequently during the third and fourth decades of life. Many cases appear at onset of the menopause. Remission of symptoms and signs is frequent after castration or when the menopause is complete. The menstrual cycles may be normal, but prolongation of the interval is not unusual. In contrast to the findings in adenofibrosis, the endometrium is often atypical. Absence of the secretory phase is a frequent finding, although hyperplasia is relatively rare.³ Many women with this disease have borne children. Lactation may be normal, but faulty lactation or premature weaning precedes the onset of the disease in many cases. Pelvic disease occurs fairly often in this group. Ovarian cysts predominate over other abnormalities. This type of lesion has been referred to as "non-puerperal secretion,"^{23, 24} "periductal mastitis," "microcystic fibroadenomatosis,"²⁵ and "benign parenchymatous hyperplasia."²⁷ Nonpuerperal secretion and associated processes, which seem to be due to endocrine dysfunction and are akin to lactation, are frequently allied with abnormalities of the process, occurring as a sequel to it as a result of incomplete involution or from the continuation of the lactation. This syndrome is probably due to an ovarian dysfunction in which the normal cyclic secretion of hormones is absent. Such a condition is suggestive of an anovular cycle, a state that often occurs in the premenopausal period when these breast lesions may make their appearance.

Unfortunately, many of the lesions seen by the clinician are not so clear cut as those described above. There may be combinations of adenofibrosis and nonpuerperal secretion. Other cases show, in addition, cyst and papillomatous formation,²⁴ which may be superimposed on the two basic processes. Such a phenomenon occurs when the less complicated lesions are of long standing and are subjected to continuous or new stimulation. This group of mixed lesions leads to great confusion in diagnosis and interpretation of causative factors. At present, because of an incomplete understanding of these types, it is difficult to evaluate possible exciting factors. Lesions resembling the various types have been produced in animals by various hormones, particularly the estrogens. At any rate, it is possible

that factors concerned in the production of the more clear-cut lesions are involved in this heterogeneous group as well.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 32401

PRESENTATION OF CASE

A sixty-three-year-old diabetic housewife entered the hospital because of abdominal swelling and pain in the right upper quadrant.

A week before admission the patient first noticed an intermittent pain in the right upper quadrant of the abdomen and occasionally a pain in the right thoracolumbar region. The pain was not influenced by food. The patient felt nauseated at times but did not vomit. The bowels moved daily in a normal fashion, and the stools became light yellow five days before admission. The urine became darker with the onset of this illness. Two days before admission the sugar reaction turned from green to brown. At the onset of the illness the patient noticed that the abdomen was increasing in size. The abdominal pain and swelling progressed gradually until the day of admission, when the pain became much severer. An injection given by a physician gave relief and the abdomen was painless at the time of entry.

The patient had had recognized diabetes for eleven years, during which she was seen frequently in the Out Patient Department. The glycosuria was usually well controlled, but six years before admission one toe became gangrenous and in the following years there were several hospital admissions for gangrene of the toes and suppuration at the sites of amputation. Early in the disease moderately increased deep reflexes of the lower extremities, bilateral Babinski reflexes and partial impairment of position and vibratory sensations were noted. There was no anemia, and the gastric acidity was normal. The last hospital stay, four months previously, had been for cellulitis of the right foot and ankle. The blood pressure had always been in the neighborhood of 190 systolic, 100 diastolic, and moderate cardiac enlargement had been present for several years. Aside from these findings and the infection, the physical examination at the last admission had been negative. The fasting blood sugar was 93 mg per 100 cc.

Physical examination showed an obese woman in no distress. The pupils were constricted and re-

sponded to accommodation, but had a paradoxical reaction to light, on former admissions they had been sluggish, but within normal limits. There were rales at the lung bases. There was a Grade I systolic murmur at the apex and base of the heart. The cardiac rhythm was regular. The abdomen was distended, and a fluid wave was elicited. Tenderness was confined to the right upper quadrant, where it was pronounced. The liver could not be definitely felt but was thought to be enlarged to the crest of the ilium. The tip of the spleen was palpable. The left fourth and fifth toes were missing, and there was a transmetatarsal amputation on the right. The legs were moderately edematous. Neurologic examination was negative.

The temperature was 98°F, the pulse 72, and the respirations 16. The blood pressure was 160 systolic, 70 diastolic.

Examination of the blood showed a hemoglobin of 15 gm per 100 cc and a white-cell count of 11,600, with 82 per cent neutrophils. The urine was yellow and had a specific gravity of 1.015. There was a +++ test for albumin, a ++ reaction for bile and a green sugar reaction. The sediment contained an occasional white cell per high-power field. The stools, which were tan and formed, gave negative guaiac reactions. The fasting blood sugar was 88 mg per 100 cc. The bilirubin was 2.2 mg per 100 cc direct, and 3.0 mg indirect. The cephalin-flocculation test was + in twenty-four hours and +++ in forty-eight hours. The total protein was 6.1 gm per 100 cc, with 4.0 gm of albumin and 2.1 gm of globulin. The nonprotein nitrogen level and the prothrombin time were normal. Abundant colon bacilli were cultured from the urine.

A paracentesis on the day after admission yielded 1500 cc. of cloudy, orange-colored fluid with a specific gravity of 1.010. There were 5400 white cells, most of which were neutrophils, and 900 red cells per cubic millimeter. Considerable fluid remained in the abdomen after the tap. The liver could not be palpated. An x-ray film showed the stomach to be distended with air. All abdominal structures were poorly outlined because of fat or fluid, or both. The spleen was slightly enlarged, but the liver shadow was not delineated. On the third day 300 cc of fluid was removed. Slight but definite icterus of the scleras and skin had appeared. The patient was apathetic and during the following day became confused. Many urine tests for sugar were blue or green, and the highest blood-sugar level was 195 mg per 100 cc. Forty units of protamine insulin were given daily. The arms and legs became cold and moist. The abdomen remained distended, and the temperature normal.

By the fifth hospital day the patient was not responsible and the jaundice of the scleras had increased. At noon the blood sugar was 261 mg per 100 cc, and the carbon dioxide 15.8 milliequiv per liter. Half an hour later she died quietly. At no

time was the pulse, respiration or temperature elevated

DIFFERENTIAL DIAGNOSIS

DR DANIEL ELLIS I do not believe that the diabetes as such was the cause of the immediate illness and death in this case. In the terminal stage there was acidosis, which I consider to have been due to whatever else the patient had and not to the fact that the diabetes was not well controlled. There is no indication of diabetic coma or diabetic acidosis.

This case, therefore, is primarily that of a woman who was known to have had diabetes, who on previous occasions had had repeated episodes of infection, and who was admitted to the hospital with a history of pain, swelling of the abdomen and increasing jaundice of approximately a week's duration. I still do not know what she had, and my final diagnosis will be given without too much conviction. The best I can do is to mention some of the possibilities.

About 50 per cent of the cases with ascites are on a cardiac basis. This woman had an elevated blood pressure, and probably had essential hypertension. There were rales at the lung bases, but the facts are stressed that at no time was there difficulty in respiration and that the pulse was not elevated or irregular. According to the record the systolic blood pressure was about 30 points below a previous reading. There was no evidence of venous distention at any time. If this patient had had cardiac failure, which might well explain the presumably enlarged liver, the abdominal pain in the region of the liver, the ascites and the edema of the feet, there should have been more evidence of the disease and of the discomfort that goes with heart failure. I cannot conceive of death from cardiac failure with the picture that is outlined here.

Cirrhosis of the liver is a possibility. The patient may have died of liver failure, but I do not believe that it was on the basis of cirrhosis. The only evidence of abnormal liver function is the cephalin-flocculation test. The prothrombin time, the serum protein, the albumin-globulin ratio, the red-cell count and the hemoglobin were normal, and the jaundice was minimal, although it gradually increased in severity. I do not believe that the terminal picture was due to portal cirrhosis or to hepatitis, which would have been an acute and fulminating one, and from the record I do not believe that an acute infectious process involving the entire parenchyma of the liver was present.

Neoplastic disease must be considered, although there is little evidence from the facts at hand. If she had cancer, it must have involved the abdominal viscera, causing obstruction of the portal circulation. Apparently there was no obstructive jaundice, no history of weight loss and no previous history of prolonged symptoms that might be attributed to a malignant neoplasm. The ascites, if caused by

cancer, could have been due either to peritoneal seeding or to obstruction of the portal vein or the inferior vena cava.

The question of infection arises. From time to time there was a chronic, suppurating process in the feet. Did the patient have amyloid disease? If the liver was enlarged, the enlargement might have been due to amyloid disease, but the fact that she had ascites to an increasing degree is slightly against it. Amyloid disease might account for the findings in the urine, however. All I can do at the moment is to mention that diagnosis as a possibility.

Could the patient have had tuberculosis? Tuberculous peritonitis might have caused such a picture, although usually with tuberculosis there is evidence of disease elsewhere. Also, the patient would probably have been febrile. The findings in the ascitic fluid are rather against tuberculosis. The fluid in a tuberculous peritonitis usually has a specific gravity of about 1.015, and the cells most frequently found are primarily of lymphocytic origin. Incidentally I should like to check the figures on the fluid. The specific gravity was 1.010, and the white-cell count was 5400. Someone must be wrong.

DR EARLE M. CHAPMAN Those are strong words, doctor. That is an important observation in this case. Where is Dr. Averill?

DR J. H. AVERILL I did the tests, and the figures are correct.

DR ELLIS That is all I wanted to know. I must say, then, that the terminal disease was one of intra-abdominal infection. Probably one of the reasons that the first paracentesis yielded only 1500 cc. of fluid is that the abdomen was large and distended and contained fluid that was pocketed, that is only an assumption, however. One might point out that the pain was due to stretching of the liver capsule, which may cause pain and on occasion simulates an acute abdominal emergency. As I mentioned previously, this type of pain, apparently severe enough to require morphine, occurs in right-sided cardiac failure or in an acute hepatitis. Possibly the morphine obscured the findings on admission. One must therefore consider the possibility of a ruptured viscus, obscured by the morphine, although I think that it is unlikely.

So far as the source of infection is concerned, I am driven back to the fact that there were repeated infections in the past, and although I am not sure that such a thing is possible, a pyelephlebitis of a septic nature may have occurred from repeated infection in the extremities. Perhaps the most logical diagnoses are a pyelephlebitis involving the liver, with septic abscesses, and peritonitis, and the terminal picture was one of overwhelming sepsis to such an extent that there was no rise in pulse rate and no great rise in the white-cell count, although the latter was definitely elevated, with 82 per cent neutrophils. The second choice is tuberculous peritonitis, with the obvious complications of diabetes,

Generalized arteriosclerosis and arteriosclerotic heart disease.

DR. WYMAN RICHARDSON I was going to discard the white-cell count and say that the patient had a glomerulonephritis initiated by a renal factor and perhaps a mild portal cirrhosis also in the background.

DR. ELLIS If a renal condition caused an illness of this degree and death, would not the nonprotein nitrogen have been elevated?

DR. RICHARDSON Was that determination made?

DR. ELLIS Yes, the nonprotein nitrogen was normal.

DR. JAMES TOWNSEND There was only one white blood cell per high-power field in the sediment. Is that not against pyelonephritis?

DR. RICHARDSON There were a ++++ test for diphtheria and abundant colon bacilli.

DR. ELLIS The albumin is consistent with acute infection elsewhere and dehydration.

DR. BENJAMIN CASTLEMAN The field is still wide open.

DR. JOHN GRAHAM I should like to ask Dr. Ellis if he has any opinion about the abnormal neurologic findings.

DR. ELLIS I could not make much out of them.

DR. GRAHAM What about the pupillary findings?

DR. ELLIS The pupillary findings on the last admission, I think, were due to morphine. The previous neurologic findings could be explained on an arteriosclerotic basis.

DR. CHAPMAN This was indeed a difficult case, and as I listened to Dr. Ellis I could appreciate how he felt. We had a disagreement on the service. There were four possibilities: heart disease, infection, cirrhosis and cancer. We excluded cardiac failure and infection, although we did not seriously entertain massive infection, as Dr. Ellis suggested. We were then left with cirrhosis and cancer and there we had the disagreement.

My interpretation was that the patient had been diabetic for years and had gone into cholemia. After the paracentesis was done we could not feel a large liver so that I interpreted it as a small, shrunken liver and thought that the cirrhosis had been present for a long time. The fluid was a transudate and not an exudate. The specific gravity was 1.010 and yet the cell count was high. How to explain this was the question. Dr. Averill took the other stand—that it was intra-abdominal cancer, with seeding throughout the peritoneum. He could not explain the low specific gravity any more than I could explain the large number of cells. Then came the point of explaining the urinary albumin. Did the patient have nephritis? I thought that she probably had a hepatorenal syndrome with a failing liver. With destruction of the liver protein massive albuminuria occurs, I should like to refer to an article by Thomas,* who calls attention to the presence of serum protein in the urine as a detoxifying process. In artificial nephritis in dogs Thomas

found that liver protein was first excreted and that tissue protein later joined the serum protein and both were excreted. With this mechanism in mind I postulated that the excessive proteins in the urine were liver and not body-tissue proteins.

DR. N. H. MARTIN† How do you explain the albumin-globulin ratio?

DR. CHAPMAN I cannot explain it.

DR. MARTIN In chronic cirrhosis the patient regenerates sufficient tissue to maintain a normal serum protein, but with loss of liver tissue the total protein ultimately drops below the maintenance level. If liver failure is acute there may be a short period when the patient lives on protein "capital," but then a fall in the total protein and a change in the albumin-globulin ratio occur, or death may come before this serum change.

DR. ELLIS Normal albumin-globulin ratios are frequently encountered in the presence of fatal hepatic damage. Within the last week we have seen a patient who died because of massive destruction of the liver by an infiltrating cancerous process. His death was obviously one of liver failure, and yet the liver-function tests a week before death were normal.

DR. TOWNSEND Dr. William C. Burrage suggests that this may have been the specific type of cirrhosis that is associated with diabetes—namely, hemochromatosis. Usually these patients have difficulty in controlling the diabetes over a long period. This history does not suggest hemochromatosis to me, but I should like to hear a discussion about that.

DR. CHAPMAN This woman had the most extraordinary pale, clear-white skin of anyone I have ever seen. We could not possibly entertain that diagnosis. It is true that she was jaundiced, but the jaundice developed only forty-eight hours before death.

DR. TOWNSEND Was the ascitic fluid examined for tumor cells?

DR. B. J. KENNEDY Yes, but no tumor cells were found.

CLINICAL DIAGNOSES

Diabetes mellitus
Cholemia
Abdominal cancer?

DR. ELLIS'S DIAGNOSES

Pylephlebitis, with multiple abscesses, of liver, portal obstruction and secondary peritonitis
Generalized arteriosclerosis
Arteriosclerotic heart disease
Diabetes mellitus, controlled

ANATOMICAL DIAGNOSES

Carcinoma of pancreas, with metastases to regional lymph nodes, liver, lungs and pleura

*Thomas, W. A. Source and role of urinary protein in nephritis. *J. A. M. A.* 97:1055, 1931.

†Of the Middlesex Hospital, London.

Thrombosis of portal vein and right hepatic artery

Massive infarction of liver, right lobe.

Infarcts of spleen and kidney

Cardiac hypertrophy, hypertensive type, mild

PATHOLOGICAL DISCUSSION

DR CASTLEMAN Autopsy showed a number of unusual findings. The heart was enlarged, weighing 450 gm. It showed mild hypertensive hypertrophy of the left ventricle. There was no evidence of heart failure. The liver was slightly enlarged, weighing 1800 gm, and presented on the surface a mottled appearance. There were numerous nodules, which seemed to be obviously carcinomatous, studded over its entire surface. They were not raised, as they usually are in carcinoma, but on cutting into them they appeared neoplastic. The liver surrounding the islands of tumor seemed softer and grayer than normal. When the liver was sectioned there was a marked difference between the right and left lobes. There was tumor in both lobes, but the intervening parenchyma in the right was soft and yellowish gray and the markings were completely obliterated, no central veins could be made out, and it had the appearance of a massive infarction. The left lobe showed tumor nodules but without any of the yellowish-gray softening, and the central veins were easily discernible. In the portal vein we found a large thrombus that extended somewhat into the splenic and somewhat into the superior mesenteric vein.

We know that portal-vein thrombosis produces partial infarction of the liver, in which one sees marked acute congestion microscopically but no necrosis of the liver cells to any degree. Ordinarily, when one finds infarction of the liver, one also expects to find a thrombus in the hepatic artery. That was looked for, and in the intrahepatic portion of the main right hepatic artery we found a fresh thrombus, which we believed to account for the complete infarction of the right lobe. There was no thrombus in the left branch. The combination of the portal-vein thrombosis and that of the right hepatic artery was probably responsible for the rapid development of cholemia. The carcinoma itself, I am sure, would not have produced the signs of cholemia. The primary source of the carcinoma was in the head of the pancreas. In addition to the liver there were metastases in most of the regional lymph nodes in the pleura and, on microscopic section, in the lung parenchyma. The source of the hepatic-artery thrombosis is still unsolved. There was a good deal of tumor surrounding the hepatic artery, and quite possibly pressure by the tumor produced thrombosis. Of course it may have been an embolus, and in favor of that theory was the finding of small infarcts in the spleen and kidney, we were unable to find any source in the aorta or heart, however.

DR WILLIAM MCK JEFFERIES Do you think that decompression from the abdominal paracentesis could have resulted in portal-vein thrombosis?

DR CASTLEMAN I do not believe so. The portal-vein thrombosis was fairly old, not so recent as the hepatic-artery thrombosis. The kidneys showed marked sclerosis, and in a few areas the glomeruli showed the intercapillary glomerulosclerosis that is seen in diabetes.

DR RICHARDSON Was there pyelonephritis?

DR CASTLEMAN No. The ascitic fluid, which was a transudate, was not due to neoplastic implants but was the result of the portal-vein thrombosis.

DR. ELLIS How about the nature of the ascitic fluid? I should like elucidation of these findings, that is, the low specific gravity and the relatively high white-cell count.

DR CASTLEMAN I do not know the answer.

DR RICHARDSON Was the specific gravity determined when the fluid was hot or cold?

DR AVERILL The test was made ten minutes after the tap, the fluid had probably cooled off somewhat.

CASE 32402

PRESENTATION OF CASE

A fifty-five-year-old Ukrainian-born restaurant porter entered the hospital because of severe hematemesis.

Eight months before admission the patient began to have a mild burning sensation in the epigastrium half an hour after heavy meals. This complaint never caused much distress or required medication. At that time he passed two black stools. A week before admission the burning sensation became worse, but was always relieved by a proprietary preparation containing bismuth. Every day for a week there were one or two loose black stools and the patient was increasingly weak. Six hours before admission on going to bed he felt weak and dizzy. He was awakened two hours later by nausea and vomited a large quantity of bright-red blood and dark clots with considerable violence. He then fainted and was unconscious for several minutes. He subsequently vomited blood once, but less violently. There was never any pain associated with the illness.

The patient had been chronically constipated for years and had lived on a diet of soup, stew and daily laxatives for the seven years before admission.

Physical examination showed the skin to be pale, dry and warm. The tongue was smooth, and the mucous membranes pale. The pulse was strong and regular. The heart, lungs and abdomen were normal, as was peristalsis.

The temperature was 98.6°F, the pulse 80, and the respirations 16. The blood pressure was 118 systolic, 65 diastolic.

Examination of the blood revealed a red-cell count

2,750,000, with 8 gm of hemoglobin, and a white-cell count of 12,500, with 90 per cent neutrophils. The urine was normal. The prothrombin time was 22 seconds (normal, 22 seconds), the nonprotein nitrogen was 47 mg and the total protein 5.3 gm per 100 cc. The stools were tarry and gave + + + + + guaiac reactions.

Whole-blood transfusions were given for two days, after which x-ray examination of the stomach and duodenum was made. The stomach was normal, but there was a defect in the duodenum that moved with peristalsis and had the appearance of a polyp. By the fifth hospital day the patient's condition was definitely worse despite 1000 cc of whole blood given daily. There was no more vomiting until the fifth day, but nausea was constant and the stools were always black. On that day the hemoglobin was 1 gm. After a transfusion the patient suddenly vomited 300 cc of blood, the pulse rose to 125, and the systolic pressure fell to 110. The pulse had returned to 100 by the next morning. The prothrombin time was 32 seconds (normal, 20 seconds), and the nonprotein nitrogen 84 mg per 100 cc. Gastric x-ray studies on the sixth day showed a normal stomach. The filling defect in the duodenum had disappeared and was assumed to have been a blood clot.

An operation was performed on the seventh hospital day.

DIFFERENTIAL DIAGNOSIS

DR. PETER SARRIS. This history is rather simple and direct in comparison with most histories that are presented here. It is equally striking by the absence of any positive data on which to make a diagnosis. In this case a diagnosis must be made by exclusion rather than by the more satisfactory method of presenting positive evidence.

Before discussing the differential diagnosis I should like to point out a few things in the history and physical examination. This eight months' story of a mild burning sensation only after heavy meals is not particularly impressive or diagnostic. Many people have a mild burning sensation after a heavy meal, especially if the meal consists of soup, stew and a daily laxative. The symptom is important, however, in view of the fact that it was associated with black stools eight months before admission. Such stools, as information given by a patient, are not always significant. When many leads are traced it is often found that the patient did not have really tarry stools. In this case the statement can be accepted because the patient later had unquestionable melena and was therefore familiar with the appearance of tarry stools. The onset can thus be dated eight months previously, but I do not find any information that helps to make a differential diagnosis. The only helpful point is the massive gastrointestinal hemorrhage. The record mentions vomiting with considerable violence. To me that

means that the stomach was probably in good tone and not one of those atonic, dilated, chronically obstructed stomachs with consequent overflow vomiting. It might also mean that the clots produced partial pyloric obstruction. The constipation I cannot tie up with the rest of the story. Once started with cathartics, the patient probably had to stick to them. That, in addition to the diet, may have been significant in producing a vitamin deficiency. I shall return to that later.

The physical examination really contributes nothing except the statement that the patient was anemic, confirming the fact that hemorrhage had occurred, and the history indicates that the patient was not in shock on admission; the pulse was 80, and the blood pressure was satisfactory.

The laboratory data are also of little assistance except to confirm the anemia. The white-cell count and the markedly increased neutrophil count confirm the recent hemorrhage. The urine was normal. I take it that that was an aggregate report. Apparently several examinations were done to exclude any urinary insufficiency or nephritis, which might conceivably tie up with the gastrointestinal bleeding. The prothrombin time was 29 seconds,—later 32 seconds,—which is slightly elevated but not in the range that would explain bleeding from a prolonged prothrombin time per se. The nonprotein nitrogen was 47 mg and later 84 mg per 100 cc, which is, of course, definitely abnormal. Anyone with major gastrointestinal bleeding, however, is entitled to it, because not only the accompanying dehydration and the periodic hypotension but also the ingestion of blood itself raise the nonprotein nitrogen, even if the patient has properly functioning kidneys and is otherwise normal. I therefore do not ascribe any particular significance to the high nonprotein nitrogen in this patient.

The course in the hospital suggests little more than that massive bleeding continued. The patient required a transfusion of 1000 cc of blood daily and after five days of this regime the hemoglobin was the same as it was on the day of admission, presumably, 5000 cc of blood had been lost in five days.

In this type of bleeding one can dispose of a number of diagnoses because of lack of evidence, such as poisoning and chronic ulceration from tuberculosis or syphilis, although in such conditions massive bleeding sometimes occurs. There is no massive bleeding with uremic ulcers and the acute ulcers that accompany acute infectious disease. Jaundice from any cause may lead to massive hematemesis. Blood dyscrasias such as leukemia and purpura also produce massive bleeding. There is no evidence of blood dyscrasias as from the blood smear, however, and it is unusual for them to cause so much gastric bleeding without evidence of a hemorrhagic tendency somewhere else. These diseases can all be excluded either because of lack of evidence or because the diagnosis can be made only when there is a

specific finding pointing to that diagnosis. The bleeding from a high prothrombin time, which I mentioned earlier, can be excluded since it was not sufficiently high in this case to produce bleeding per se, although it might have contributed to the aggravation of the bleeding. Furthermore, in cases of bleeding due to an elevated prothrombin time, jaundice or sepsis is almost always apparent as the cause.

The source of bleeding can be limited to a location between the lower esophagus and the duodenum. The combination of melena and hematemesis fairly well limits the lesion to that area, which of course is a large area and can include a great deal of disease. In the course of bleeding from duodenal ulcer melena usually precedes hematemesis and often there is only melena, whereas in bleeding from the esophageal varices the reverse is true.

Once in a while one sees massive hemorrhage from a gallstone that has perforated into the duodenum, usually from a gangrenous gall bladder. There was no evidence of gall-bladder disease in this case, and certainly such an episode of perforation into the duodenum would have been accompanied by pain, which was absent. In such cases, the bleeding is incidental.

One more cause, idiopathic bleeding, when nothing else is found, can be excluded. In some patients with repeated and marked bleeding even after part of the stomach is resected the bleeding continues and no explanation is ever found. I do not believe that that is the answer in this case. Presumably, Dr Mallory will confront us with some pathologic lesion. Cancer, peptic ulcer, esophageal and gastric varices, gastritis and benign gastric tumors remain.

It might be wise to see the x-ray films at this point.

DR MILFORD D SCHULZ: The x-ray films taken in this case are missing.

DR SARRIS: I think it fair to ask, then, if the roentgenologist was satisfied with the second film showing a completely normal stomach and duodenum, excluding the possibility suggested by the first film of a polyp that might have receded into the fundus of the stomach and therefore become invisible.

DR SCHULZ: That is a possibility, of course, but the fact that the disappearing lesion was assumed to be a blood clot indicates a careful search for some explanation.

DR LEWIS K DAHL: I might amplify Dr Schulz's remark by saying that Dr Schatzki considered his examination to be reasonably satisfactory.

DR SARRIS: I take it that gastroscopy was not done and that it was regarded as inadvisable.

DR TRACY B MALLORY: I believe that that is true.

DR SARRIS: I also take it that no cellular studies were made on the gastric contents. Such studies are becoming increasingly valuable for early diagnosis.

DR MALLORY: No such information is given.

DR SARRIS: I believe that gastric cancer is the

least likely diagnosis. First of all, it accounts for only 5 per cent of the massive hemorrhages, and there was no suggestive history, there was no weight loss, and no weakness except after massive bleeding. Furthermore, I believe that a gastric cancer is not likely to have been missed by x-ray examination.

Peptic ulcer must be more seriously considered because it accounts for 75 per cent of massive hemorrhages of this type. The history is reasonably consistent with it, although the burning sensation was mild only after heavy meals. I do not recall seeing such a massive hemorrhage from duodenal ulcer in which some deformity of the duodenum—a crater, spasm or a similar lesion—was not demonstrated by x-ray examination. This patient had two examinations. The lesion could have been a small peptic ulcer in the stomach, which is sometimes missed in the x-ray film.

Esophageal varices, which account for 5 to 10 per cent of massive hemorrhages of this type, are secondary to cirrhosis, hepatic insufficiency or previous portal or splenic thrombosis. Many patients enter the hospital for the first time because of massive bleeding from esophageal varices, and the diagnosis of portal cirrhosis is made. Usually, some abnormality, such as an enlarged spleen, is disclosed by the physical examination or by laboratory tests, such as liver-function studies, which were not done in this case. The most important feature against esophageal varices is the x-ray film, which rarely misses them. Gastric varices offer a different problem, since they can be missed by x-ray examination. I remember a case with repeated hematemesis in which several x-ray films were taken and nothing was demonstrated. At operation, performed with Dr Richard H Sweet, the patient was found to have varices limited to the fundus. Gastric varices must therefore be considered, but there is no evidence for the disease that produced the varices. Gastritis, with single or multiple erosions, which has been encountered in several cases, could well have been present, the erosions being superficial and peptic in nature but not deep enough to produce a lesion visible on x-ray study.

The last consideration is benign gastric tumor, which includes adenoma, leiomyoma, hemangioma, neurogenic fibromas and lipoma. Excessive bleeding is characteristic of such tumors, particularly the adenomas, the leiomyomas and the hemangiomas. They may be pedunculated, and when I first read this history, before I reached the last paragraph, it seemed certain that the diagnosis was an adenoma that had prolapsed into the duodenum. That is why I was anxious to determine the possibility of a polyp. But the roentgenologists apparently believed that the possibility of a polyp that receded into an invisible position was much less than that of a blood clot. Therefore, if this was a benign tumor of the stomach, there was no conclusive x-ray evidence.

In conclusion the diagnosis depends on the consideration of which lesion that I have mentioned is not only frequent enough to be considered but also easiest to be missed by x-ray examination. Benign tumors are often overlooked unless they are large or have a large ulceration, which they sometimes do. If the tumors are small and are not deeply ulcerated they are missed because they do not disturb peristalsis and do not usually produce spasm and because the mucosal pattern is often normal. I cannot make any final decision. If it turns out to have been a benign tumor, the adenomas and leiomyomas are the commonest occurrence. The bleeding tumors most frequently encountered are the hemangiomas and the adenomas, which are my first choice. My second choice is a gastritis, with single or multiple superficial erosions. My third choice is gastric varices.

DR. EDWARD B. BENEDICT: Nine times out of ten, in a massive hematemesis, one would be correct in saying that the lesion was a benign peptic ulcer. I cannot quite agree with Dr. Sarris about the x-ray finding. I can recall 3 cases within a few years with massive hematemesis in which, in spite of an entirely negative x-ray examination, benign peptic ulcers were present.

DR. SARRIS: In the stomach?

DR. BENEDICT: Yes, in the stomach. In 1 case, in which the ulcer was prepyloric, gastroscopy demonstrated nothing. Another ulcer was in the upper part of the stomach, and the patient was not gastroscopied. The third was in the midpart, and gastroscopy a month before operation showed gastritis but did not show the tiny ulcer that was bleeding.

DR. SARRIS: The point that Dr. Benedict has made is well taken. I included a small benign peptic ulcer with the diagnosis of gastritis with single or multiple superficial erosions, because the small benign gastric peptic ulcers are to me similar to the superficial erosions in some cases of gastritis. Both conditions are often missed by x-ray examination.

CLINICAL DIAGNOSIS

Leiomyoma of stomach

DR. SARRIS'S DIAGNOSIS

Benign gastric tumor

ANATOMICAL DIAGNOSIS

Cirsoid aneurysm of left gastric artery, with secondary peptic erosion

PATHOLOGICAL DISCUSSION

DR. MALLORY: We hardly expected Dr. Sarris to make the diagnosis because this case presented a lesion that is unique in the experience of this laboratory.

Will you tell what you found at operation, Dr. Hamlin?

DR. EDWARD HAMLIN, JR.: On opening the abdomen we found the upper gastrointestinal tract filled with blood and nothing else. We thought seriously for a time that we were dealing with idiopathic bleeding, which Dr. Sarris mentioned. The third part of the duodenum and the stomach were carefully inspected. We opened the stomach along the antrum and found a great deal of blood and nothing else. While we were cogitating — the



FIGURE 1 Photomicrograph of the Large Eroded Vessel in the Submucosa, with Thrombus Formation

stomach was suspended between forceps — we noted blood accumulating in the upper part of the stomach, and that limited the field. Going over it carefully again we found a minute, actively bleeding speck, which was partially blood clot, about two thirds of the way from the pylorus to the fundus on the posterior wall. This was resected.

DR. MALLORY: The gross specimen that we received showed a small projecting red mass, which was evidently a thrombus overlying an artery in the submucosa. On dissecting the specimen further it was evident that an unusually large branch of the left gastric artery — as large as the main artery itself — came up through the muscularis into the mucosa for a distance of perhaps 0.5 cm and then turned around and bent down again to penetrate the muscularis once more. This vessel was sclerotic and tortuous, and we classified it as a cirsoid aneurysm. The mucosa over the artery and one side of its wall were entirely eroded away (Fig. 1). I suppose that the pressure of this abnormally large vessel immediately beneath the mucosa had led to ulceration of the mucosa, peptic in character, with the subsequent massive hemorrhage.

Whether this represents a congenital abnormality of the vessel or a developmental one I do not know any way of determining.

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REALISM VERSUS WISHFUL THINKING

Organized medicine in this country has become increasingly conscious that a large section of the public holds it in low regard. This has been a disturbing thought to the leaders in the profession, as well as to the rank and file, and the average physician is apt to inquire why it is that, although as an individual he seems to be well thought of by those he serves, his collective acts, as expressed through the organizations that he and his colleagues comprise, are held in such low esteem. Is the physician a dual personality—a sort of Dr. Jekyll when serving the public in his individual capacity and Mr. Hyde when he acts in concert with his fellows?

Has organized medicine lost its democratic character? As a matter of fact, the pattern of democracy nowhere in this country is more closely followed

than it is in the conduct of the business of the majority of medical societies. Who can truthfully say that the House of Delegates of the American Medical Association is not concerned in the democratic spirit, either in its formation, in the methods attending its deliberations or in the conclusions it arrives at? If this body does not follow the democratic plan, neither then does the Congress of the United States, after which it was and continues to be closely patterned.

Can it be said that the democratic process has ceased to function in the Massachusetts Medical Society? Here, again, over the years democracy has grown and expanded. As an example, three of its most important committees—the Committee on Public Relations, the Committee on Legislation and the Executive Committee of the Council—are composed of a representative of each of our eighteen district societies. It may well be that the apparent ill repute of the Society in the minds of the public is conditioned by the indifference that some physicians show toward the conduct of the Society's affairs. This does not, however, connote a real lack of support any more than does the average citizen's attitude of indifference to the actual management of his government.

There seems to be little to support the dual personality theory. Nor does it seem likely that organized medicine has fallen in esteem because the public believes that it has ceased to walk in the democratic way.

At a meeting of the House of Delegates of the American Medical Association held in July at San Francisco, the delegates were informed of a particular activity that had been conducted under the auspices of the Board of Trustees, which took notice of the suspicions regarding public relations. A firm prominent and skilled in determining public opinion was engaged to determine whether these suspicions had any foundation in fact and if so what was to be done about it. On the one hand, this effort confirmed the popularity of the individual physician, and on the other, the low esteem in which he and his fellows are held as an organized group.

In an endeavor to find the answer to what seemed like a contradiction, those making the survey examined the entire setup of the American Medical Association. They found in the various scientific

activities of the organization so much in the interest of the public good as to constitute a veritable gold mine from the standpoint of public relations but they also learned that the public knew nothing about such treasure. Most people had heard of the American Medical Association, but principally as an organization that was working for the defeat of such legislation as the Wagner-Murray-Dingell Bill

The advice looking toward the remedy of this situation was simple. The people should be told about these scientific activities all of which are so definitely in their interest. They should be told in a language that is easily understood, they should be told at times that are opportune, and they should be told often. It should, however, be recognized that, although this remedy is simple, its proper application requires the services of a person with special experience and skill and that the job will be well done in proportion to the training and ability of the person selected to do it.

The program thus outlined was adopted by the House of Delegates. Whoever is chosen to carry out the plan will work in close harmony with the secretary and the general manager of the American Medical Association and with all its various bureaus and councils.

This is an experiment that offers much promise. It is realism as opposed to wishful thinking, it properly recognizes the value of a well informed public — an asset that has been developed by many organizations during the past ten or twenty years. State medical societies should watch this experiment closely, for in its operation may be found the answer to certain of their own difficulties.

TOXICITY OF TRIDIONE

INFECTIOUS diseases are not the only ones that benefit from chemical research. Even the Hippocratic disease, epilepsy, profits from the synthesis of new compounds. Latest encouragement comes from the use of a drug, 3,5,5-trimethylvloxazolidine-2,4 dione, the trade name of which is Tridione. The therapeutic peculiarity of this chemical is its nearly specific effect on a particular group of seizures, the so-called "petit-mal triad" — petit mal, akinetic seizures and myoclonic jerks. In one group of 166

patients treated at the Children's Hospital in Boston, two thirds were freed or almost freed of this particular type of seizure. Grand-mal seizures, on the other hand, were not helped and often became more frequent. Because the drug is of specific value for clinical syndromes associated with the alternate spike and wave of the electroencephalogram, it offers intriguing opportunity for further studies.

The more high-powered the weapon of offense, the greater the possibilities of harm if it should backfire. Peculiar reactions may accompany the use of Tridione. Generalized skin rashes are frequent but do not become serious if the drug is discontinued promptly and reinstated gradually. Photophobia (hemeralopia) is a peculiar, but apparently harmless, side effect for which there is as yet no explanation. A more disquieting complication is the occasional appearance of blood dyscrasias. Symptomless leukopenia or eosinophilia has been noted in a few patients,¹ and in two cases recently reported there was aplastic anemia with agranulocytosis, uncontrollable bleeding and death.^{2,3}

An allergic or toxic reaction of a patient to a given drug is always a lively possibility. Withholding medicines that have ever caused serious reactions would work misfortune on the many who require those medicines. Tridione medication has resulted fatally for only one of some 5000 patients being treated. This ratio can be increased if physicians, forewarned, will take the necessary precautions. These are as follows: prescribe Tridione only for the type of seizure that can be helped, — namely, petit mal (pykno-epilepsy), myoclonic jerks and akinetic seizures, — and for patients without a history of blood dyscrasia, give no more than the amount needed to control petit mal, inquire for weakness, pallor, dyspnea, undue bleeding and hemorrhagic skin eruptions, and examine the blood monthly and stop medication if the platelets are substantially reduced, if the white-cell count falls below 4000 or the percentage of neutrophils below 50 per cent or if there is pronounced anemia. Having taken these precautions, the physician can give tridione to his young patients who are subject to petit mal with the expectation that approximately two thirds of them will receive substantial relief from this type of seizures.

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MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

ALMY — Thomas Almy, M.D., died September 6. He was in his sixty-third year.

Dr. Almy received his degree from Harvard Medical School in 1909. He was formerly chief of the staff of Union Hospital, and was a member of the New England Obstetrical and Gynecological Society and the New England Pediatric Society and a fellow of the American Medical Association. He was a diplomate of the American Board of Obstetrics and Gynecology.

His widow survives.

BAILEY — Marshall H. Bailey, M.D., of Norwell, died September 18. He was in his eighty-eighth year.

Dr. Bailey received his degree from the College of Physicians and Surgeons, Baltimore, in 1893.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR AUGUST, 1946

RÉSUMÉ

DISEASES

	AUGUST 1946	AUGUST 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	62	127	24
Chancroid	0	1	*
Chicken pox	123	121	121
Diphtheria	20	11	11
Dog bite	1045	974	1031
Dysentery bacillary	1	54	15
German measles	46	38	38
Gonorrhea	365	459	426
Granuloma inguinale	1	0	*
Lymphogranuloma venereum	0	1	*
Malaria	16	68	6
Measles	400	274	281
Meningitis meningococcal	4	6	6
Meningitis, Pfeiffer-bacillus	2	1	1
Meningitis, pneumococcal	0	1	1
Meningitis staphylococcal	0	2	1
Meningitis, streptococcal	0	0	0
Meningitis other forms	2	4	1
Meningitis undetermined	3	1	1
Mumps	142	312	271
Pneumonia, lobar	29	93	77
Salmonella infections	45	48	22
Scarlet fever	112	157	195
Syphilis	310	293	354
Tuberculosis, pulmonary	246	215	260
Tuberculosis other forms	19	12	23
Typhoid fever	6	4	8
Undulant fever	6	5	5
Whooping cough	498	531	508

*Made reportable December, 1943

†Four-year average

COMMENT

Diseases reported at an incidence above the seven-year median included anterior poliomyelitis, diphtheria, German measles and measles.

Although above median prevalence, poliomyelitis had an incidence of about half that of last year.

Diphtheria showed the highest August prevalence of the last ten years. This is the fourth consecutive month in which such an increase has taken place.

Diseases reported below the median prevalence included meningococcal meningitis, mumps, scarlet fever and whooping cough.

Lobar pneumonia was again at a record low for the seventh consecutive month.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Arlington, 1, Auburn, 1, Beverly, 1, Blackstone, 1, Blandford, 1, Boston, 5, Brookfield, 3, Carlisle, 1, Dedham, 1, Framingham, 1, Franklin, 1, Harwich, 1, Holyoke, 1, Hull, 1, Lancaster, 1, Lowell, 3, Lynn, 1, Lynnfield, 1, Malden, 2, Marblehead, 1, Medford, 1, Methuen, 1, Middleboro, 1, New Bedford, 1, North Adams, 1, North Attleboro, 2, Northampton, 3, Norwood, 1, South Hadley, 1, Somerville, 1, Walpole, 1, Washington, 1, Watertown, 2, Wellesley, 1, Weston, 1, Worcester, 13, Wrentham, 1, total, 62.

Diphtheria was reported from Boston, 10, Braintree, 1, Cambridge, 1, Mansfield, 1, New Bedford, 2, Somerville, 3, Sudbury, 1, Waltham, 1, total, 20.

Dysentery, amebic, was reported from Quincy, 1, total, 1. Dysentery, bacillary, was reported from Boston, 1, total, 1. Lymphocytic choriomeningitis was reported from Agawam, 1, total, 1.

Malaria was reported from Boston, 7, Bourne, 2, Cambridge, 2, Clinton, 1, Haverhill, 1, New Bedford, 1, Oxford, 1, Somerville, 1, total, 16.

Meningitis, meningococcal, was reported from Boston, 2, Canton, 1, Lawrence, 1, total, 4.

Meningitis, Pfeiffer-bacillus, was reported from Beverly, 1, Medford, 1, total, 2.

Meningitis, other forms, was reported from Springfield, 1, total, 2.

Meningitis, undetermined, was reported from Amesbury, 1, Salem, 1, Shrewsbury, 1, total, 3.

Rocky Mountain spotted fever was reported from Dennis, 1, total, 1.

Salmonella infections were reported from Beverly, 3, Boston, 2, Chelsea, 1, Lawrence, 1, Lynn, 23, Malden, 1, Marblehead, 5, Newton, 2, Peabody, 1, Quincy, 1, Springfield, 1, Swampscott, 1, Topsfield, 1, Winchester, 1, Yarmouth, 1, total, 45.

Septic sore throat was reported from Boston, 7, Brookline, 1, Greenfield, 1, Holbrook, 1, Newburyport, 1, Somerville, 1, total, 12.

Tetanus was reported from Quincy, 1, total, 1. Trichinosis was reported from Boston, 2, Norwood, 1, total, 3.

Typhoid fever was reported from Boston, 2, Chicopee, 2, Marblehead, 1, Randolph, 1, total, 6.

Typhus fever was reported from Malden, 1, total, 1.

Undulant fever was reported from Adams, 1, Dighton, 1, New Ashford, 1, Southbridge, 1, Westminster, 1, Worcester, 1, total, 6.

BOOK REVIEWS

Anatomy as a Basis for Medical and Dental Practice By Donald Mainland, M.B., Ch.B., D.Sc., F.R.S.E., F.R.S.C. 8°, cloth, 863 pp., with 61 illustrations and 11 tables. New York: Paul B. Hoeber, Incorporated, 1945. \$7.50.

It is refreshing to read a textbook of anatomy, such as this, written in a manner that retreats from the conventional method of presentation. Students of medicine and dentistry will find a copy of this book an asset throughout their professional career. A student, soon to begin a course in anatomy, will find himself well oriented in this subject matter if he carefully reads and perhaps rereads Part I, which succinctly discusses the aims and methods of anatomic studies, and then turns to Appendix III, to become acquainted with important hints on how to read and write articles pertaining to anatomy. Armed with the understanding that these chapters will supply, the student is led to the study of Part II, presenting general anatomy, which begins with a considera-

tion of the body as a whole and proceeds to the discussion of bones, joints, muscles and fascias, blood and lymphatic vessels, nerves, skin and appendages. Part III concerns regional anatomy, the upper and lower limbs, thorax, abdomen, head and neck, back, brain and spinal cord and the autonomic nervous system. The reviewer wishes to draw special attention to the appendices, which deal with subjects such as radiology, postnatal ossification of limbs, normal weights of organs, tooth eruption dates, adult pelvic dimensions and segmental cutaneous nerve supply. Excellent references are given for each chapter, and a good index is supplied.

The volume as a whole has much merit and the author succeeds in offering his readers a well written, instructive and provocative book.

The Autobiography of Science. Edited by Forest R. Moulton, Ph.D., Sc.D., and Justus J. Schifferes. 8°, cloth 666 pp. Garden City, New York: Doubleday, Doran and Company, Incorporated, 1945. \$4.00.

It may be said that science had its beginnings in the recording of astronomical observations in Babylonian times, twenty centuries before the beginning of the Christian Era, and that its development has been international in scope, embracing all peoples and languages.

The compilers of this autobiography of science have brought together selections of all countries and all times—from the hieroglyphics of the ancient Egyptians and the *Old Testament* story of the Creation to the modern period of Osler, Cannon and Cushing. The book is fundamentally an anthology of the key passages from the master works of all sciences.

From an original list of three hundred authorities it was found necessary, because of space limitation, to reduce the number to a hundred, and in so doing the compilers were guided by two criteria: their importance as turning points in the history of science and their readability. They also attempted to determine the best thing a person ever wrote about the most important thing he or she ever did, the greatest consideration being given to persons whose work seemed to chart the main stream of the development of scientific thought. Three of the authors quoted are women: Lady Mary Wortley Montagu, Florence Nightingale and Madame Curie. The selections are in general arranged in chronological order by periods under eight headings, beginning with 'Science Is Born (Antiquity)' and concluding with 'Science Sires the Twentieth Century'.

The original texts of fifty-five of the selections, which were in a language other than English, are presented in translations by modern scholars, with the single exception of Cuvier, of whose work a new translation is offered. For the most part the writings are in simple words, easy to understand and to follow in their context. Only eleven of the scientists quoted write in a manner that is slow or hard to read. It is the impression of the compilers that there are fewer than a hundred unusual scientific words among the more than two hundred and fifty thousand words comprising the volume. In only one instance, Einstein, was it considered necessary to provide a special vocabulary.

In preparing the texts for publication the general reader has been kept in mind rather than the specialist, and the final editing has been done in the style of the best current American usage. Mathematical notation and symbolism have been omitted, but mathematical reasoning and theory necessary to the theme have been included.

The selections of each author quoted are preceded by a short biographic commentary.

Of the selections, fifty are on biologic and medical subjects, and of this number thirty-four are medical or of medical interest. The second selection quoted comprises excerpts from the Egyptian, Edwin Smith and Ebers papyri. The second to the last selection is Harvey Cushing's quoted "Homo Chirurgicus," which is given in full. The medical selections are all from outstanding, well known names in medicine: Hippocrates and Galeo in antiquity, Gui de Chauliac and the Regimen Sanitatis of Salerno in the Middle Ages, Leonardo da Vinci, Paracelsus, Fracastorius, Paré, Vesalius and Harvey in the Renaissance, Leeuwenhoek and Fauchard, the dentist, in the seventeenth and early eighteenth centuries, and Benjamin Franklin, Lady Montagu, Jenner, Laënnec, John Snow, Beaumont, Holmes, Crawford Long, W. T. G. Morton,

Pasteur, Lister, Florence Nightingale, Sedgwick, Roentgen, Freud, Osler, Cannon and Cushing in the later years.

This book may be used as a reference and source book, as a narrative or as a textbook on the history of science. It should be in all libraries, public and private, general and special, and is especially recommended for all medical libraries and for all persons interested in the history of medicine.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Way of an Investigator: A scientist's experiences in medical research. By Walter B. Cannon, M.D. 8°, cloth 229 pp. New York: W. W. Norton and Company, Incorporated, 1945. \$3.00.

The late Dr. Cannon, in this semipopular book, has written an autobiographical account of his work and at the same time has given a description of how the scientific investigator goes about doing his job.

Pulmonary Edema and Inflammation: An analysis of processes involved in the formation and removal of pulmonary transudates and exudates. By Cecil K. Drinker, M.D., D.Sc., professor of physiology, School of Public Health, Harvard University, Boston. The Nathalie Gray Bernard Lectures delivered at the Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, North Carolina, in December, 1944, together with a fifth chapter on artificial respiration. Monograph No. 7, Harvard University Monographs in Medicine and Public Health. 8°, cloth, 106 pp., with 27 illustrations. Cambridge: Harvard University Press, 1945. \$2.50.

Dr. Drinker analyzes the formation and removal of pulmonary transudates and exudates. He also discusses the prevention and treatment of lung edema, and in the final chapter he reviews the problems and techniques of artificial respiration.

The Bacterial Cell: In its relation to problems of virulence, immunity and chemotherapy. By René J. Dubos, George Fahyao Professor of Comparative Pathology and professor of tropical medicine, School of Medicine and School of Public Health, Harvard University, and member of the Rockefeller Institute. With an addendum by C. F. Rohinow, Straughways Laboratory, Cambridge, England. Monograph No. 6, Harvard University Monographs in Medicine and Public Health. 8°, cloth, 460 pp., illustrated. Cambridge: Harvard University Press, 1945. \$5.00.

This important book describes the organization of the structural and physiologic components of the bacterial cells and interprets the phenomena of virulence, immunity and chemotherapy in terms of cellular organization. The present study utilizes not only direct microscopic methods but also the information derived from indirect methods, based on the physicochemical, physiologic and immunologic behavior of bacteria. This monograph should be in all medical and biologic libraries. An extensive bibliography is appended to the text.

Physical Chemistry of Cells and Tissues. By Rudolf Höber, University of Pennsylvania School of Medicine. With the collaboration of David I. Hitchcock, Laboratory of Physiology, Yale University School of Medicine, J. B. Bateman, Mayo Clinic, David R. Goddard, University of Rochester Biological Laboratories, and Wallace O. Febo, University of Rochester School of Medicine and Dentistry. 8°, cloth, 676 pp. Philadelphia: The Blakiston Company, 1945. \$9.00.

This comprehensive monograph is divided into eight principal sections. The first is devoted to a discussion of selected principles of physical chemistry applicable to the study of cell physiology. The following sections on the molecule, protoplast, cellular activity, respiration, contractility, passive penetration and active transfer to animal and plant tissues. The work is well documented, with selected references to the subject, and has adequate author and subject indexes. This monograph should be in all medical and related libraries.

A Manual of Surgical Anatomy By Tom Jones and W C Shepard Prepared under the auspices of the Committee on Surgery Division of Medical Sciences, National Research Council 4th, cloth, 195 pp, illustrated Philadelphia and London W B Saunders Company, 1945 \$5 00

This latest of the series of military surgical manuals is without text and has been prepared especially for surgeons in the field

Clinical Biochemistry By Abraham Cantarow, M D, professor of physiological chemistry, Jefferson Medical College, and Max Trumper, Ph D, Lt Commander, H(S)USNR, Naval Medical Research Institute, National Naval Medical Center, Bethesda, Maryland Third edition, revised 8th, cloth, 647 pp, with 29 illustrations Philadelphia and London W B Saunders Company, 1945 \$6 50

This authoritative textbook has been thoroughly revised to incorporate the progress in biochemistry during the five years that have elapsed since the publication of the second edition The volume considers many new tests and new subjects, including classifications of jaundice, physiology of gastric and pancreatic secretion and methods for the study of deficiency in the various vitamins, a chapter dealing with hormone assay and endocrine function has been added The authors have attempted to present controversial subjects in an impartial manner, supplemented by an expression of personal opinion The last chapter constitutes an outline of chemical abnormalities in various disorders, with pertinent page references A comprehensive index concludes the volume Selective bibliographies are attached to each chapter The material is well organized, and this book should prove valuable for reference purposes

NOTICES

ANNOUNCEMENTS

Dr Thomas W Botsford announces the opening of his office for the practice of general and pediatric surgery at 1101 Beacon Street, Brookline

Dr Donald T Chamberlin announces the opening of his office at 422 Beacon Street, Boston, for the practice of diseases of the digestive system

Dr Frederick C Irving announces the removal of his office to 1180 Beacon Street, Brookline

Dr John Ellis Knight announces his return from service with the armed forces and the reopening of his office at 520 Commonwealth Avenue, Boston

Dr L Tillman McDaniel announces his return to the practice of internal medicine at 12 Bay State Road, Boston

Dr James F McDonough announces the opening of his offices for the practice of obstetrics and female diseases at 15 Dix Street, Winchester, and 1101 Beacon Street, Brookline

Dr Elsie S Neustadt announces the opening of an office for the practice of psychiatry and neurology at 27 Avon Way, Quincy

Dr Ian P Rak announces his return to the practice of psychiatry and neurology at 422 Beacon Street, Boston

Dr Eugene Suzedell announces his return from military service and resumption of practice at 59 Coddington Street, Quincy

Dr Aldo G Verde, having returned from service with the United States Navy, announces the opening of his office for the general practice of medicine and surgery at 676 Adams Street, Dorchester

VAN METER PRIZE AWARD

The American Association for the Study of Goiter again offers the Van Meter Prize Award of three hundred dollars and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland Provided essays of sufficient merit are presented in competition, the award will be made at the annual meeting of the association, which will be held in Atlanta, Georgia, on April 3, 4 and 5, 1947

The competing essays may cover either clinical or research investigations, should not exceed three thousand words in length and must be presented in English, a typewritten double-spaced copy should be sent to the corresponding secretary, Dr T C Davison, 207 Doctors' Building, Atlanta 3, Georgia, not later than January 1, 1947 The committee that will review the manuscripts is composed of men well qualified to judge the merits of the competing essays

A place will be reserved on the program of the annual meeting for presentation of the winning essay by the author if it is possible for him to attend The essay will be published in the *Proceedings* of the association This will not prevent its further publication, however, in any journal selected by the author

JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a m

MEDICAL CONFERENCE PROGRAM

Friday, October 4 — Aggressive Behavior — Its Psychiatric and Physiologic Aspects, Especially in Combat Veterans
Dr Leo Alexander

Wednesday, October 9 — Iodine Metabolism Dr John VanderLaan

Friday, October 11 — Hepatic Function with Respect to Bromsulphalein Removal Dr Franz J Ingelfinger

Wednesday, October 16 — Tuberculous Lesions of Bones and Joints Dr Arthur A Thibodeau

Friday, October 18 — Recent Studies in Hemorrhagic Shock
Dr Arnold M Seligman

Wednesday, October 23 — Massachusetts Medical Society
Dr Dwight O'Hara

Friday, October 25 — Pituitary Adrenal Relations Dr R O Greep

Wednesday, October 30 — Homologous Serum Hepatitis
Dr William Maloney

On Tuesday and Thursday mornings, Dr S J Thannhauser will give medical clinics on hospital cases On Saturday mornings, clinics will be given by Dr William Dameshek Medical rounds are conducted each week day by members of the staff from 12 00 to 1 00 in the Lecture Hall
All exercises are open to the medical profession

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The annual meeting of the New England Obstetrical and Gynecological Society will be held in Boston on Wednesday, October 30, with headquarters at the Hotel Somerset.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The regular fall meeting of the New England Oto-Laryngological Society will be held in conjunction with the Massachusetts Eye and Ear Alumni on Wednesday, November 20, at 11 a m at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston

(Notices continued on page xii)

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SCARLET FEVER

An Epidemiologic and Bacteriologic Study of Cases Occurring in a Small Community

A. DANIEL RUBENSTEIN, M.D.,* AND GEORGE E. FOLEY†

BOSTON

THE serologic classification of the hemolytic streptococcus has often been applied to the study of more or less circumscribed outbreaks of scarlet fever and other streptococcal infections¹⁻⁴ and to the investigation of samples of endemic cases occurring during the so-called "streptococcus season" in a given community.⁵⁻⁸ There are, however, relatively few reports in which all or nearly all the endemic cases of scarlet fever occurring in a community have been studied bacteriologically as well as epidemiologically.

Perhaps the most complete information on the scarlet fever occurring in individual communities during a stated period is contained in the report of Schwentker, Janney and Gordon,⁹ who performed bacteriologic and epidemiologic studies on scarlet fever in several villages in Rumania.

Studies in schoolrooms¹⁰ and in families¹¹ suggested the hypothesis that the variety of serologic types of hemolytic streptococci recovered from patients when scarlet fever is endemic may be composed of innumerable so-called "pure-type" outbreaks occurring in basic units of the population.⁵⁻⁸ The sudden appearance of scarlet fever in a rural community that, except for a single case, had been free of this infection for a year was regarded as an excellent opportunity for further investigation of the transmission of this disease, the serologic classification of the hemolytic streptococci being utilized at the same time.

GENERAL DESCRIPTION

Ipswich, where the present studies were done, is a community with a population of 6611, situated on the northern coast of Massachusetts. Milk is supplied by several dealers, some of whom market raw milk. In 1945 the town had a total of 930 school children in attendance at four elementary

schools (three public and one parochial) and one high school. A single local theater attracts children from several surrounding communities. Children are discouraged from attending the theater when contagious diseases are prevalent and school is in session, but there are no restrictions during vacation or recess periods.

During the interval between January 2 and May 24, 1945, a total of 94 cases of scarlet fever was reported from this community, in contrast to 1 case reported in 1944 and 15 cases reported in 1943. Cases were scattered throughout the community, with no correlation with any of the various milk routes. Interestingly enough, one of the early cases due to Type 1 hemolytic streptococci occurred in a milk dealer who distributed raw milk, and several subsequent cases due to the same serologic type of hemolytic streptococcus occurred among the consumers of his product. His milk, however, had been removed from sale. At this time, Type 1 cases were appearing among persons taking milk from several other local and outlying dealers. Without complete investigation the original situation could have been misleading.

The original purpose of this study was to isolate and classify the hemolytic streptococci from all the cases occurring in the community. For one reason or another, throat cultures could not be obtained in certain cases. Of those cultured, Group A hemolytic streptococci¹² were isolated from 71 or 76 per cent of all the cases occurring in the community. The serologic types of these strains were classified according to Griffith's¹³ slide-agglutination technic. The incidence of the various types is summarized in Table 1. The distribution of types in this community is not unlike that previously reported from certain other Massachusetts communities in 1942-1943⁸ and 1944.¹⁴

The onset of cases by ten-day periods according to serologic type is represented in Figure 1. Cases occurring in 1943 and 1944 are represented schematically. The curve presents two distinct peaks,

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†Technical associate in epidemiology, Department of Preventive Medicine, Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health.

each composed of cases due to several different serologic types

CASES IN SCHOOLROOMS

The first case appeared on January 2 in a child who attended Grade 3 of School 1. Type 2 hemo-

TABLE 1 *Distribution of Serologic Types of Hemolytic Streptococci Isolated*

TYPE OF STREPTOCOCCUS	NO. OF CASES	PERCENTAGE
2	25	35
1	22	31
19-24*	10	14
6	7	10
10	4	6
8	2	3
9	1	1
Total	71	

*Cross agglutination with the serums used

lytic streptococci were isolated from this case. Within the next nine days 7 additional cases due to Type 2 appeared among the children in the same schoolroom. Concurrently, on January 4 and 5, 2 cases due to Type 19 hemolytic streptococci developed, and on January 6, 2 cases due to Type 1 also

In contrast to the abrupt outbreak in Grade 3, School 1, cases in the other grades and schools were scattered, sometimes only 1 or 2 cases were reported from a grade or school. Unlike the schoolroom outbreaks previously reported¹⁰ there was no striking correlation between serologic type and schoolroom, primary cases due to different types occurred in the same room, and each type produced secondary cases in the same and other schoolrooms, as well as in nonschool contacts (Table 2).

As would be expected, 71 cases (76 per cent) occurred in children of school or preschool age. The attack rates for scarlet fever in the various schools of the community varied from 0.1 to 16.8 per cent (Table 3). The rate for school children was 5.0 whereas that for preschool children was 3.7 per cent.

Of the 71 cases occurring in school and preschool children, only 38 (54 per cent) could be accounted for by direct case-to-case contact. These contacts, together with extraschool cases secondary to schoolroom cases, are shown in Figure 2.

CASES IN FAMILIES

All cases reported during the period of the study occurred in 49 families. Sixteen families (33 per

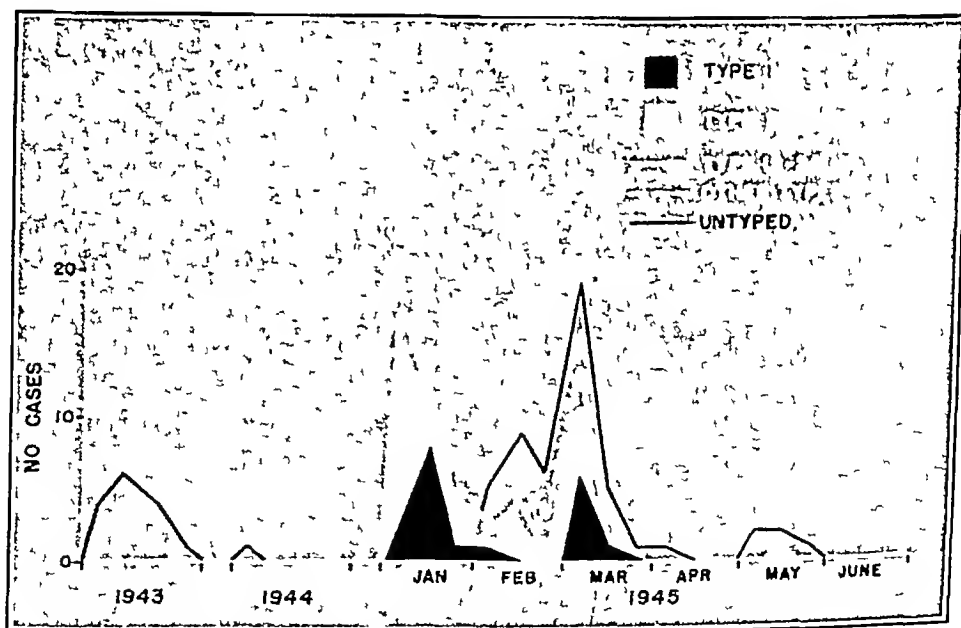


FIGURE 1 *Distribution of Cases of Scarlet Fever by Serologic Type*

appeared in this schoolroom. No cases were reported from this schoolroom after January 9.

On January 10 cases began to appear in other grades of the same school and, later in the same month and throughout February, in other schools in the community. Scarlet fever remained prevalent in the other grades of this school and in other schools during the winter and spring months.

cent) accounted for 58 cases (64 per cent). The hemolytic streptococci causing scarlet fever in 14 of these 16 families were classified according to serologic type (Table 4).

As previously observed¹¹ the hemolytic streptococci recovered in the cases occurring in a given family were invariably of the same serologic type, indicating that the secondary cases were the result

of household exposure The intervals between the onset of the primary and secondary cases occurring in these families are shown in Table 5 It is noteworthy that more than a third of the secondary cases occurred more than twenty-one days after the primary case—the usual period of isolation for

scarlet fever due to more than one type of hemolytic streptococci had occurred, multiple infections within a given family were due to a single serologic type This correlation of type with family is in striking contrast with the lack of correlation of type with schoolroom shown in Table 2 Further-

TABLE 2 Serologic Types of Hemolytic Streptococci Producing Scarlet Fever in Nonschool Contacts of Schoolroom Cases

CASES	TYPE OF STREPTOCOCCUS	WINSHIP SCHOOL GRADE						BURLY SCHOOL	SHATTSWELL SCHOOL	FRENCH SCHOOL	HIGH SCHOOL	TOTAL
		1	2	3	4	5	6					
School primary	1			2								2
	2			1								2
	6							2				2
	8								1			
	9										1	1
	10								1			1
School secondary	19-24*										1	1
	1	3	1	7				1		1		7
	2	4	2†									11
	6							1			1	1
	8											1
	9											1
Totals	10											
	19-24*	1	1	2	2	1†	1		1		1	8
		8	1	12	2	0	1	4	3	1	5	37
Nonschool secondary	1	4	4	5								13
	2	2		3					2			7
	6							2				2
	8											
	9											
	10								3			3
Totals	19-24*										1	1
		6	4	8				2	5		1	31†

*Cross-agglutination with the serums used
†Untyped cases in families in which other cases were all of this type
‡Includes 5 Type-2 cases in a family with no school contact

scarlet fever According to our method of determining the interval between cases,* several secondary cases were as long as one hundred and thirty-two days removed from the primary case The role of the family in the spread of scarlet fever is further emphasized by the correlation of

more, the appearance of cases due to a particular serologic type of hemolytic streptococci in a given schoolroom in many cases was shown to be the result of family spread from a child attending some other grade or school

CASES WITH SOURCE ESTABLISHED

It has been reported that the hemolytic streptococci causing illness in a given group are usually of a serologic type not previously present in the population⁴ The heterogeneous type composition of endemic scarlet fever suggests multiple introductions of types previously not present in the community, in contrast to the introduction of a single type producing a well defined outbreak¹ Whether the sudden increase from a single case in 1944 to 9½ cases in the winter and spring of 1945 was due to a more or less general absence of hemolytic streptococci or of particular serologic types in 1944 followed by multiple introductions in 1945 cannot be stated definitely, since carrier rates were not studied Two fairly clear-cut cases were established, however, in which scarlet fever was introduced into the community from outside sources

One patient developed scarlet fever on the evening of the day he arrived home from California Within the next two weeks, three family contacts (2 adults and 1 preschool child) and a next-door neighbor, who came to visit the patient, developed scarlet fever

TABLE 3 Attack Rates of Scarlet Fever

CHILDREN	NO OF STUDENTS	NO OF CASES	ATTACK RATE %
School children	1020	51	5.0
Winship	179	30	16.8
Burley	184	7	3.8
Shattswell	189	3	1.6
French	90	1	0.1
High school	378	10	2.6
Preschool children	536	20	3.7
Totals	1556	71	4.5
Average			

serologic types of hemolytic streptococci recovered from the primary and secondary cases occurring in a given family irrespective of the schoolroom attended by the patient with the primary case In Table 6 school and nonschool secondary cases are divided according to family and school attended by the patient with the primary case and then arranged according to serologic type Although 1 or more of the children in each family attended schools in which

*In a theoretical family, Cases a, b and c occur Time intervals ab, ac and bc are included in Table 5

All cases were due to Type 2 hemolytic streptococci. The other child in the family who attended school was not ill, and was carrying Type 1 hemolytic streptococci in the throat. Although these cases were due to a type that had already appeared elsewhere in the community, in view of the data on multiple infections in families, there is little doubt

These cases, together with those occurring in schools and families for which a source of infection could be established, comprised 73 per cent of all cases occurring in the community (Table 7). If the 53 cases occurring as multiple infections in 14 families are omitted, however, only 16 (39 per cent) of the remaining cases can be accounted for by

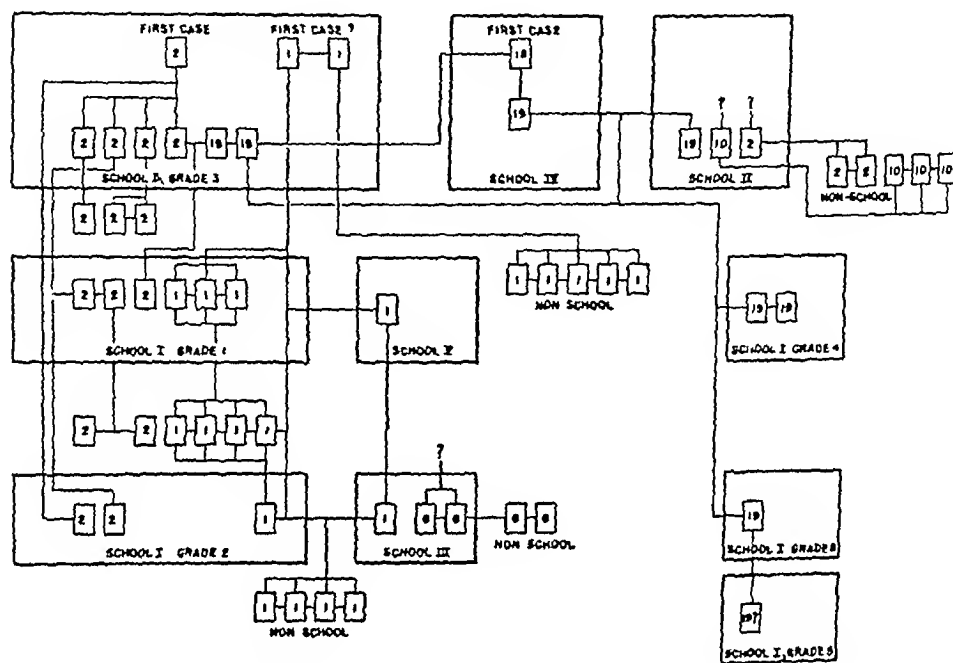


FIGURE 2 Diagrammatic Representation of Spread of Scarlet Fever among School and Preschool Children

that the patient infected his family after he himself had been infected while en route home from California.

Another patient developed scarlet fever on the afternoon of the day he arrived home after several months' absence as a naval recruit. Type 8 hemolytic streptococci were isolated from nose and throat cultures. There was only 1 other case due to this

recognized contact, even with fairly detailed bacteriologic and epidemiologic studies.

DISCUSSION

The role of the schoolroom^{10, 15} and the family unit^{14, 16} in the genesis of scarlet fever, as well as

TABLE 4 Serologic Types of Hemolytic Streptococci Isolated from Multiple Cases in Families

TYPE OF STREPTOCOCCUS	NO. OF FAMILIES	NO. OF CASES
2	7	22*
1	1	17
19-24†	1	6
10	1	4
6	1	4

*1 case not typed occurred in a family in which all other cases were Type 2.

†Cross agglutination with the serums used.

TABLE 5 Intervals between Multiple Cases in Families

INTERVAL, Days	NUMBER OF CASES	PERCENTAGE
0	7	7
1-7	27	28
8-14	19	20
15-21	7	7
22-132	36	38
Total	96	

type, which occurred in a young woman who lived across the hall from the patient. These infections developed late in the spring, near the end of the streptococcus season, otherwise it is conceivable that other cases might have originated from the patient.

in other infectious diseases,¹⁷ is more or less established. The present study seems to be of particular interest in that, although the primary cases appear to have originated in the schoolroom, familial contact was the principal factor in maintaining the spread of the disease. Not only did a few families account for most of the cases occurring in the community but also the appearance of a case due to a given type in a schoolroom could sometimes

accounted for by familial contact with a patient attending another schoolroom. The consistency with which a given type was recovered in all cases occurring in a family indicates that familial contact, rather than chance exposure to the same type of organism outside the home, was usually responsible for spread of infection. This was true not in-

comprising secondary waves were often caused by several serologic types. Since outbreaks of streptococcal infection usually result from the introduction of a type not previously present in the population, the sudden appearance of cases due to three different serologic types in this community suggests multiple introductions of new types

TABLE 6 Correlation of Serologic Types of Hemolytic Streptococci Recovered from Primary and Secondary Cases in Families

FAMILY No	TOTAL PRIMARY AND SECONDARY CASES	PROBABLE SOURCE OF PRIMARY CASE	NUMBER OF CASES OF TYPE				
			1	2	6	10	19-24*
1	6	Winship (Grade 3)	6				
2	4	Winship (Grade 3)	4				
3	7	Winship (Grade 3)	7				
4	3	Winship (Grade 3)		3			
5	3	Winship (Grade 3)		3			
6	3	Winship (Grade 3)		3			
7	3	Winship (Grade 3)		3			
8	3	Winship (Grade 3)		3			
9	3	Winship (Grade 3)		3			
10	4	Shattswell					
11	4	Burley			4		
12	4	Shattswell				4	
13	3	High school					4
14	6	High school					2
Totals	53	?	17	22	4	4	6

*Cross-agglutination with the serums used

frequently in spite of the fact that the child who contracted scarlet fever attended a schoolroom in which cases due to other serologic types of hemolytic streptococci were occurring.

In several cases only a single case of scarlet fever appeared in a given schoolroom (Fig 2). Since data on the Dick status of the children in these schoolrooms were lacking, it cannot be said that there were available susceptibles. As has been observed, however, the exhaustion of susceptibles is not the sole reason for the cessation of an outbreak of scarlet fever,^{9, 10} and the lack of susceptibles is not the only explanation why an outbreak does not occur or continue to occur in a population unit infected with a suitable strain of hemolytic streptococci. The same phenomenon has been observed in studies of measles,¹⁷ in which the introduction of a case into a population known to contain susceptibles did not give rise to secondary cases. The element of chance is perhaps a factor in such cases, for example, if the patient is exposed only to immune persons before being segregated, no new cases develop. In scarlet fever, furthermore, it is known that all susceptibles (as judged by the Dick test) who acquire the epidemic strain during the course of an outbreak do not develop clinical illness.^{9, 10}

The data presented above differ from the studies by deVaal¹⁵ and our previous experience with scarlet fever in schoolrooms¹⁰ where the majority of cases in a given schoolroom was due to a single serologic type. Griffith¹⁸ observed that although in schools the cases occurring in primary epidemic waves were usually due to a single type, the cases

or else some unknown mechanism. Despite the multiplicity of human contacts complicating the epidemiology of scarlet fever, however, 2 cases were established in which the introduction of disease-producing streptococci into the community from outside sources was followed by secondary cases within the community.

Unlike Griffith's¹⁸ studies the appearance of different serologic types as the cause of disease did

TABLE 7 Cases with Known Source of Infection

Source	No of Cases
School contact	37
Extrascchool familial contact	29
Extrascchool nonfamilial contact	1
Extra-community contact	2
Total	69

not appear in distinct waves but occurred almost simultaneously (Fig 1), the type composition of each of the peaks of high incidence being essentially the same. The type pattern in this community was not unlike that previously observed in different localities in Massachusetts,^{5, 14} suggesting a fairly widespread distribution of the predominant types producing scarlet fever, and fluctuated only in relatively large units of time and space.

Although it is known that the ability to produce erythrogenic toxin is a characteristic easily acquired or lost,⁵ there is no exact explanation why certain types suddenly appear in a community and attain predominance over other serologic types as a cause of streptococcal disease. Nor is the disappearance

of such a strain from the community clearly understood, for example, there is no adequate explanation for the absence of scarlet fever during 1944 in the community considered, although at the same time the type pattern producing disease in 1945 was present in other Massachusetts communities during 1943-1944.^{5, 14} And there is no satisfactory explanation for the sudden appearance of 94 cases in this community in 1945, with type patterns similar to those previously observed elsewhere.

The succession of seasonal changes appears to be intimately related to the biology of the hemolytic streptococcus, or to its host-parasite relation. The times of high and low incidence of scarlet fever, for example, occur with surprising regularity over a period of several years.¹⁴ Season seems to be a factor common to nearly all outbreaks of streptococcal disease, regardless of type composition, the majority occurring during the winter and early spring months. Griffith's¹⁸ observation that the danger periods of school outbreaks in England are the Christmas and Lent terms applies equally to the observations made in this country. The heterogeneous type composition of endemic scarlet fever, with the parallel seasonal fluctuations in the prevalence of the predominant as well as the sporadic types recorded here and elsewhere,¹⁴ suggests the operation of some factor other than serologic type in the spread of this disease.

SUMMARY

Between January 2 and May 24, 1945, a total of 94 cases of scarlet fever occurred in a community with a population of 6611 as compared with 15 cases reported in 1943 and 1 case in 1944. The hemolytic streptococci isolated from 71 (76 per cent) of these cases were classified according to serologic type. Seven types were encountered. Types 2, 1, 19, 6, 10, 8 and 9 in order of frequency. The type pattern was similar to that previously observed in other Massachusetts communities during the period when the present community was experiencing little scarlet fever.

Seventy-one cases (76 per cent) occurred in children of school and preschool age. The first case appeared in Grade 3 of School 1 and was followed by a sharp outbreak of 11 additional cases in that room. Types 2, 1 and 19 appeared almost simultaneously in this schoolroom. Cases in other rooms of the same school were followed by the appearance of the disease in other schools in the community.

In the entire outbreak 49 families were involved. Of these, 14 contributed 53, or 64 per cent, of all the cases occurring in the community. In each case multiple infections in the same household were due, to the same serologic type. Familial contact accounted for the appearance of sporadic cases in various schools other than those in which the primary cases originated.

There was no correlation between serologic type and schoolroom attended, but there was a correlation between serologic type and family. This suggests that although infection was introduced into the family from the schoolroom, familial contact was the principal factor in maintaining spread.

Other than multiple infections in the same household, a source of infection could be established with the help of serologic classification in only 16 (39 per cent) of the remaining cases.

We acknowledge the assistance of Dr Robert E Archbald, district health officer, Massachusetts Department of Public Health, Dr Frank Collins, chairman, Board of Health, Ipswich, Mr Paul Jodoin, agent, Board of Health Ipswich, and Mrs Jerome Meyer, R.N., School Department, Ipswich.

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ACUTE SALPINGITIS DUE TO *FRIEDLÄNDER'S BACILLUS*

Report of a Case

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IT is the purpose of this paper to report a case of acute salpingitis in an eighty-year-old woman, caused by *Klebsiella pneumoniae*. Acute suppuration of the fallopian tube in elderly women is rare, and salpingitis due to this organism is doubly unusual. Extrapulmonary *K pneumoniae* infections have received increasing attention in published reports during the last few years. In 1937 Baehr, Schwartzman and Greenspan,¹ reporting a study of 198 cases found only 6 (3.5 per cent) with infection in the vagina, uterus or adnexa. Other cases of Friedländer-bacillus infections of the female genital tract have been reported by Scheyer,² Reichert³ and Hepp.⁴

CASE REPORT

Mrs B H, an 80-year-old widow, entered the Surgical Service of the Peter Bent Brigham Hospital on October 21, 1945, complaining of lower abdominal pain of 6 hours' duration. In 1938 a diagnosis of diverticulosis had been made on barium-enema studies by the family physician. About 6 hours before entry, while riding in a car, the patient experienced a sudden pain just below the umbilicus that quickly shifted to both lower quadrants. The pain was severer on the left than on the right side and was steady in character but was not severe enough to double her up. She was nauseated but did not vomit. She had had a normal bowel movement shortly before the onset of the pain. There had been no changes in bowel habits, and she had noticed no blood or pus in the stools. The bowels had moved once daily with the occasional use of milk of magnesia.

The past history revealed that the patient had undergone a cholecystectomy in 1934 for cholelithiasis. In 1941 she was treated on the Medical Service of the Peter Bent Brigham Hospital for unresolved lobar pneumonia of the right upper lobe. She had subsequently been followed carefully by the family physician, who had examined her sputum on numerous occasions and had found no tubercle bacilli. She had never had hemoptysis and brought up little sputum. In December, 1942, a check-up chest film was reported to show dense fibrous tissue in the right upper lobe with a cavity. Findings were thought to be compatible with an organizing Friedländer-bacillus pneumonia with residual cavity. No Friedländer's bacilli had ever been isolated from the sputum.

There was no family history of typhoid fever, diabetes, tuberculosis, cancer or blood diseases.

Physical examination showed a thin woman lying in bed in no apparent distress. The rectal temperature was 99°F, the pulse 84, and the respirations 26. The blood pressure was 132/82. The chest was clear except for diminished breath sounds over the right upper lobe. The heart was not enlarged, and the sounds were regular and of good quality. The peripheral arteries were firm and tortuous on palpation. The abdomen was moderately distended, and peristalsis was diminished. There was tenderness over the entire lower abdomen but more marked in the left lower quadrant. Involuntary muscular spasm was present in the left lower quadrant, and rebound tenderness was referred. No masses were palpable. Rectal and pelvic examination showed tenderness on the left, but no masses were palpable. The uterus was small, and there was no pain on movement of the cervix.

Examination of the blood showed a hemoglobin of 12.0 gm and a white-cell count of 17,600. The blood smear showed 78 per cent neutrophils, 18 per cent lymphocytes and 4 per cent monocytes. Urinalysis was not remarkable. The blood urea nitrogen was 9 mg., and the plasma protein 6.5 gm per 100 cc., the chloride was 85 milliequiv per liter.

The provisional clinical diagnoses were diverticulitis, with pelvic peritonitis, unresolved pneumonia of the right upper lobe and arteriosclerosis of the peripheral arteries.

The patient was observed for 8 hours, during which a plain film of the abdomen and a chest film were made. The former was essentially negative, and the latter showed extensive pulmonary fibrosis with a cavity in the right upper lobe similar to that reported in the chest film made in 1942. A



FIGURE 1 Low-Power Photomicrograph of Fallopian Tube
Note the diffuseness of the inflammatory reaction

Miller-Abbott tube was passed because of the diminished peristalsis and abdominal distention. At the end of the period of observation the tenderness and spasm in the left lower quadrant had increased, and the temperature had risen to 101.2°F by rectum. The white-cell count rose to 23,000. Because of these changes operation was carried out about 8 hours after entry.

Laparotomy under ether anesthesia was performed through a left-lower-quadrant, rectus-muscle-splitting incision. A moderate amount of thick exudate was present in the pelvis,

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and the sigmoid showed numerous diverticulums covered by thick plaques of fibrin. The left fallopian tube overlay the lower sigmoid, and its distal two thirds was markedly swollen and inflamed. The fimbriated end of the tube was attached to the sigmoid, and when it was freed, thick yellow pus escaped. A left salpingectomy and sigmoidostomy were performed, and the wound was closed around the loop of sigmoid without drainage. Cultures of the pelvic exudate and pus from the fallopian tube grew a Type A Friedländer's bacillus. The postoperative diagnoses were acute salpingitis of the left fallopian tube, acute diverticulitis of the sigmoid and pelvic peritonitis.

After operation the course was uneventful. The Miller-Abbott tube was removed on the 3rd postoperative day. The patient was afebrile by the 5th postoperative day. She received 4 gm. of sulfadiazine daily, a blood level between 10 and 15 mg. per 100 cc. being reached. This was discontinued on the 16th postoperative day. The patient was discharged

and serosal layers of the tube to be diffusely infiltrated by polymorphonuclear leukocytes (Fig. 1). The lumen of the tube was distended by exudate made up, for the greater part, of polymorphonuclear leukocytes and containing large numbers of bacteria (Fig. 2). Stains showed these bacteria to be encapsulated, short, gram-negative bacilli.

The fact that Type A strains of Friedländer's bacillus were cultured from the sputum, the pelvic cavity and the fallopian tube is suggestive evidence that the lungs were the portal of entry for the organism in this case. Julianelle,⁶ in a study of eight strains of *K. pneumoniae* gathered from various sources found that 52 per cent were Type A, 15 per cent Type B, 9 per cent Type C and 24 per cent Group X. It is of interest to note that 70 per cent of the Type A strains were associated with pneumonia in human beings. Similarly Perlman and Bullowa⁷ and Solomon⁸ reported series of cases of Friedländer-bacillus pneumonia in which the Type A strains were the infecting organisms in the great majority. Recently Kinney and Ginsberg⁹ stressed the significance of serologic typing of Friedländer's bacillus, and reported 7 cases of liver abscess in which all the organisms except one belonged to other groups than Type A. They further pointed out that Type A, in their experience, was usually associated with respiratory infections. These studies add supportive evidence to the thesis that the patient first suffered from a Friedländer-bacillus pneumonia, and that the tubal infection was metastatic from the lungs.

The sulfonamides have been used in the treatment of *K. pneumoniae* infections with varying results. Heilman¹⁰ reported the use of streptomycin in experimental infections, with encouraging results. Herrell and Nichols¹¹ have stated that they successfully used streptomycin in 45 patients. The patient reported above was treated with sulfadiazine, but the pulmonary infection was unaffected. It must be emphasized that localized infections should be treated surgically in the same fashion as any pyogenic infection. The patient responded well to salpingectomy and drainage of a wound abscess, both associated with a Type A Friedländer's bacillus. She was not given streptomycin, but Herrell and Nichols¹¹ mentioned 4 cases of ozena due to Friedländer's bacillus in which the symptoms were relieved by intramuscular streptomycin in total dosage of 9,600,000 to 14,000,000 units over a period of several days.

SUMMARY

A case of acute salpingitis due to Friedländer's bacillus occurring in an eighty-year-old woman is reported. The patient was treated by salpingectomy with recovery. A Type A Friedländer's bacillus was recovered from the sputum, peritoneal cavity, fallopian tube and a postoperative wound abscess. It is suggested that the lungs were the primary focus of infection. The literature is briefly reviewed.

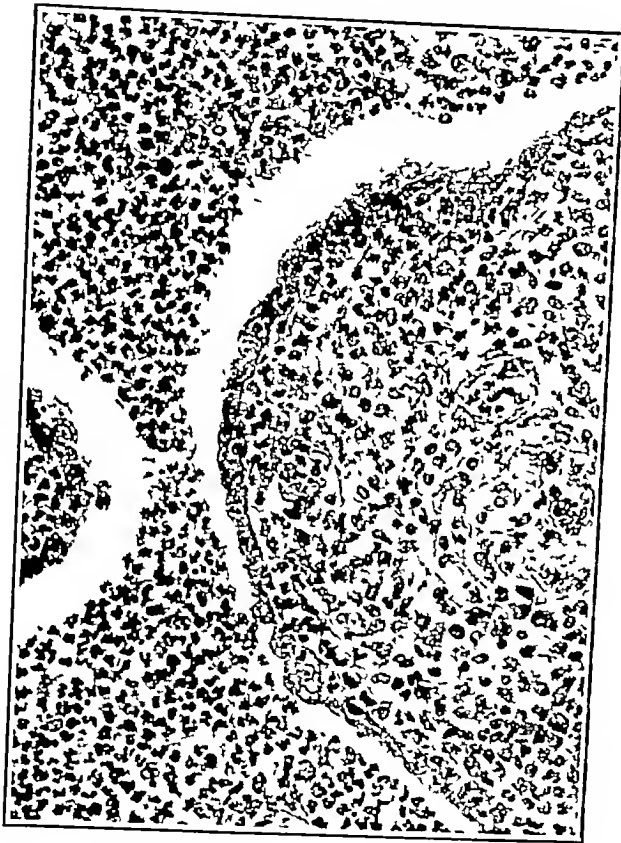


FIGURE 2 High-Power Photomicrograph of Fallopian Tube
This shows the nature of exudate in the lumen of the tube

on the 20th postoperative day, when the colostomy was functioning well and she was asymptomatic. A check-up 2½ months later showed her to be still doing well. A culture of the colostomy at that time grew no Friedländer's bacilli, but she had developed a small abscess in the operative wound, which was drained. A Type A Friedländer's bacillus was recovered from the culture. The organism was also isolated from the sputum for the first time.

The left fallopian tube measured 7 cm. in length. The diameter of the tube varied from 0.7 to 1.9 cm. The distal two thirds of the tube was swollen and tense, and its serosal surface was dark red and covered by many patches of waxlike fibrinous exudate. The fimbriated portion was ragged and inflamed and covered by exudate. The muscular layers of the tube were swollen. The lumen was patent and was distended by the presence of a large quantity of soft, thick, yellow-white exudate. The mucosa was dull red and ulcerated in places. Microscopic sections showed the muscular, mucosal

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THE CAUSE, RELIEF AND PREVENTION OF HEADACHES ARISING FROM CONTACT WITH DYNAMITE

FIRST LIEUTENANT ARTHUR M SCHWARTZ, MC, AUS

AS EARLY as 1910 Laws¹ described the so-called "Nitroglycerin head," and several papers soon followed that helped to elucidate the physiologic effects of nitroglycerin on the human body, especially after the absorption of extremely minute quantities through the unbroken skin, or even the inhalation of the fumes when dynamite is used for blasting purposes.²⁻⁴

Men working in powder plants soon acquire a rather transient immunity to nitroglycerin that can rapidly be lost over a period such as a weekend or during a vacation. Return to the job consequently results in a severe headache, which is also experienced by men first starting to work with dynamite. Such men subsequently discover that the application of a small amount of dynamite within the sweatbands of their hats provides a sufficient immunity to lessen the likelihood of a headache after prolonged contact with dynamite. The headache and its associated symptoms are so severe that it is not unusual for the men to be somewhat irritable, pugnacious and difficult to get along with. A case of homicide has been reported in which a man experiencing a severe dynamite headache drank an alcoholic beverage, which increased the dilatation of the intracerebral vessels and greatly magnified the headache. A display of maniacal manifestations is not unusual.^{5, 6}

With the advent of war it was necessary for many large groups to be exposed to the handling of dynamite and other demolition agents, particularly "C₁." The following report is based on a study conducted at a Pacific combat training center, where considerable quantities of dynamite were dealt with daily to simulate battle conditions and adequately to prepare troops for engagement with the enemy.

Primary interest was in a group of 10 men whose principal duty involved intimate contact with dynamite (20 per cent nitroglycerin), and whose subsequent complaints were intense throbbing headache, nausea, some vomiting and occasional tremors of the upper extremities. Between 8:00 and 11:00 a.m. each man was required to handle several hun-

dred sticks of dynamite. At noon on the same day the 10 men frequently reported to the post dispensary because of intense, severe, debilitating headaches, they wanted something to relieve the throbbing, the tenseness of the scalp, the nausea and the sensation that the top of the head was "ready to blow off."

The problem was approached on the basis of the following considerations: the cause of the headache, the degree of psychogenic element present in its development, possible drugs or combinations of drugs to reduce the severity of the headache once initiated, and prophylaxis to eliminate or diminish the occurrence of the headache.

It is interesting that these men actually dealt with two distinct types of explosives. C₂, a substance closely allied to trinitrotoluol with an oily base, which is molded to fit around such a structure as a pillbox and must be detonated with some form of cap, and dynamite, which contains 20 per cent nitroglycerin and can be exploded by dropping from a suitable height or striking with a heavy object. All men, at one time or another, had witnessed a serious accident from a dynamite explosion involving loss of limb or life — the possible psychogenic factor is obvious. Some form of controlled experiment was required to prove the identity of the offending substance. Patch tests in which dynamite was used and similar ones employing C₂ were prepared. The patch, which contained enough dynamite to cover the surface of a dime, was applied to the back over the left scapula of 15 men reporting for morning sick call, these men, who were told nothing of the nature of the substance applied to their backs, had complained of symptoms in distant, unrelated portions of the body. Fourteen subjects returned three hours later complaining of severe throbbing headaches, associated with a feeling of warmth over the face, and some nausea, and 1 reported the appearance of scintillating bodies in the right visual field. These men were given two aspirin tablets with no relief. In several cases the severity of the symptoms was increased. None of the 15 subjects tested with C₂

complained of headache after the passing of an equal period

What are the mechanisms and the physiologic processes involved in a nitroglycerin headache? Ten subjects who handled dynamite were skin tested with an intradermal injection of 0.01 mg of histamine (0.01 cc of a 1:1000 solution), approximately 90 per cent developed a marked cutaneous reaction, with pseudopodia and much erythema. In fact, this minute quantity was sufficient in one subject to reproduce the headache described under the influence of dynamite. Goodman and Gilman⁷ state that nitroglycerin and nitrites produce an increase in intracranial pressure that is principally due to cerebral vasodilatation, but do not make clear whether the intracerebral or extracerebral vessels are involved. Schumacher and Wolff,⁸ differentiated headaches arising from dilatation of the arteries of the scalp and dura and those due to dilatation of the intracerebral vessels. The histamine headache, which is included in the latter group, is relieved by an increase in the cerebrospinal-fluid pressure effected either by pressor drugs or by direct raising of the pressure. In contrast, the headache that is present in migraine and hypertension and is produced by dilatation of the vessels of the scalp and dura is not affected by an increase in the cerebrospinal-fluid pressure, which merely increases the difficulties when one considers the action of nitroglycerin on the cerebral vessels.

From all available sources and from personal observation it appears that the headache produced by contact with nitroglycerin is closely analogous to that caused by histamine injection. Examination of the fundi at the height of the headache tends to support this claim. The retinal vessels — especially the arteries — of all subjects reveal marked dilatation. With histamine injection a similar vasodilatation of intraocular vessels is observed. All but 1 of the 10 subjects displayed a substantial hypotension, the systolic blood pressure varying between 85 and 110 at the time of the dynamite headache, the normal average systolic pressure for this same group was 119. This lowered arterial pressure is associated with a proportionately reduced spinal-fluid pressure.⁹ Relief of the headache requires a drug with vasoconstricting and pressor effects, which subsequently tends to elevate the cerebrospinal-fluid pressure.

Gottlieb¹⁰ was principally concerned with the vasoconstricting and concomitant pressor action of amphetamine (Benzedrine) sulfate in migraine attacks. In addition, this drug reduces the amplitude of the pulsations of the cranial arteries. As in the migraine syndrome, the headache of nitroglycerin causes extreme fatigue and mental slowness. In many cases adequate performance of simple daily tasks is impossible. Gottlieb administered amphetamine sulfate intravenously and aborted the migraine attack but considered small repeated doses necessary to prevent a recurrence.

A series was set up in which 10 subjects who had never handled dynamite were given amphetamine sulfate orally, 5 mg in the early morning and 10 mg at noon. This schedule was carried out three days before the initial contact with dynamite. The subjects were subsequently given the patch test with dynamite described above. None of the group complained of headache after three hours of continuous exposure to 20 per cent nitroglycerin. Some of the usual side actions of amphetamine were noted including difficulty in falling asleep and a moderate amount of nervousness.

Pelner and Aibel¹¹ obtained gratifying results in 66 patients with periodic and histamine headaches who were given gradually increasing doses of prostigmine bromide orally. Acetylcholine was believed to be a factor in the headache, and desensitization with

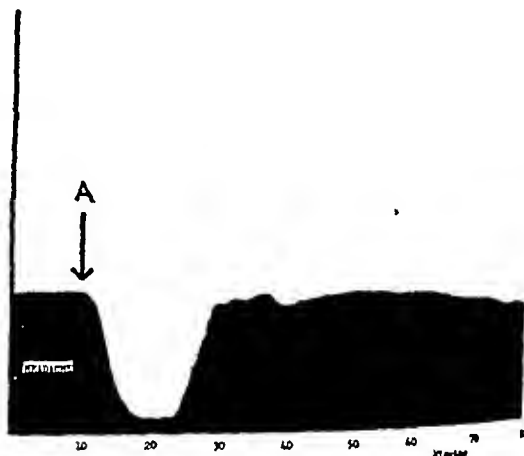


FIGURE 1 The Effect of Adrenalin

This graph represents the effect of the injection of 0.5 cc of a 1:1000 adrenalin solution (A) on the average subject with a nitroglycerin headache. The patient experiences immediate relief from the severe headache, but within the passing of a few minutes the symptoms return and in many cases are more pronounced than before the injection.

oral prostigmine bromide was considered possible. The 10 subjects in the series who continuously dealt with dynamite had a common denominator, namely, a marked local cutaneous reaction to intradermal histamine injection. Histamine is a substance with physiologic properties similar to those of acetylcholine. Intradermal injection of either drug produces dilatation of cerebral vessels. Prostigmine, which is an inhibitor of cholinesterase and can mobilize the acetylcholine reserves of the body, lessens the reaction when histamine is released outside tissue cells. One might speculate whether histamine is released in persons in contact with nitroglycerin.

The purpose was to expose the subjects to gradually increasing doses of prostigmine bromide. Forty-five milligrams of the drug was dissolved in 60 cc of water, and the men were instructed to take one drop

n the morning, two at noon and three at night on the first day. An increase of one drop for each dose was ordered until thirty drops had been taken, when thirty drops daily for an entire week, and subsequently thirty drops three times a week, were taken. When the men were receiving thirty drops three times weekly, they were asked to handle dynamite continuously for a full day without the usual precautions, that is, rubber gloves. During the time when they were taking prostigmine bromide the men were not in contact with dynamite. This was necessary to ensure against any transient immunity that might be developed from contact with dynamite. At the completion of a full day's work with dynamite only 20 per cent of the group complained of headache, and this was of a nature that did not require medication for relief.

Early in the study a method of obtaining immediate relief for these men whose assignment brought them in continuous daily contact with dynamite

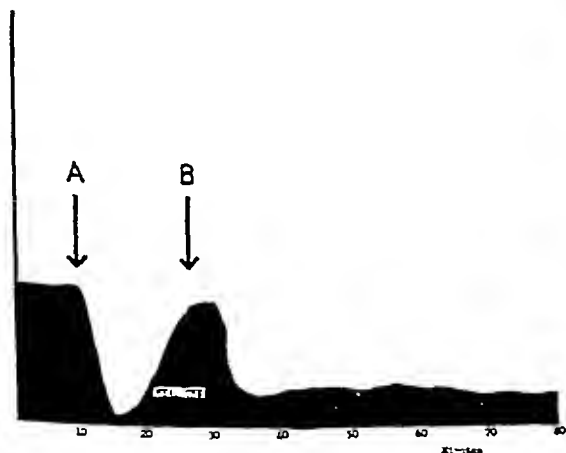


FIGURE 2 The Effect of Ergotamine Tartrate

This graph represents the immediate and later effects of two injections of 0.25 mg of ergotamine tartrate (A and B), spaced fifteen minutes apart, on the average subject with a nitroglycerin headache.

was sought. A drug with marked vasoconstricting and pressor effects, such as adrenalin, caffeine sodium benzoate, ergotrate, amphetamine sulfate or ergotamine tartrate, appeared to be required. Such analgesics as aspirin, phenacetin, codeine and the barbiturates were without beneficial effect and in many cases increased the severity of the headache and other symptoms. Adrenalin, in a dose of 0.5 cc of a 1:1000 solution, produced transitory relief lasting only several minutes and was soon followed by an increase in the symptoms, possibly owing to the vasodilating effect following vasoconstriction (Fig 1). Ergotrate, in a dosage of 0.2 mg, likewise produced only a momentary obliteration of the headache. After receiving the ergotrate several subjects experienced increased nausea and abdominal cramps—a frequent side action of ergotrate. Ergotamine tartrate,¹² in a dosage of 0.25 mg subcutaneously

was given and produced lasting relief in about 40 per cent of the subjects and a transient effect in 60 per cent (Fig 2). The greatest relief for the headache caused by contact with nitroglycerin was obtained with an intramuscular injection of 0.5 gm of caffeine sodium benzoate, followed by 5 to 10 mg of amphetamine sulfate orally (Fig 3). The systolic blood pressure and the cerebrospinal-fluid pressure rose after a subcutaneous injection of amphetamine sulfate. This is significant because in a nitroglycerin headache there is a reduced arterial pressure and subsequently a reduced spinal-fluid pressure.

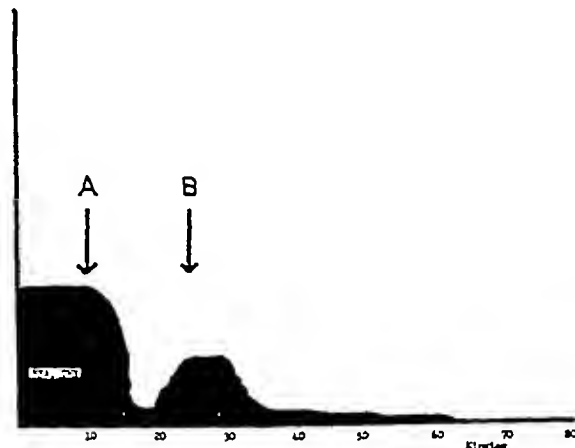


FIGURE 3 The Effect of Caffeine Sodium Benzoate followed by Amphetamine Sulfate

This graph represents the effect of the intramuscular injection of 0.5 gm of caffeine sodium benzoate (A), followed in fifteen minutes by the oral ingestion of 5 to 10 mg of amphetamine sulfate (B), on the average subject with a nitroglycerin headache. This combination gave the best results.

sure. About an hour after the ingestion of 10 mg of this drug a moderate rise in the systolic blood pressure, with marked relief of the headache, was observed.

Several laboratory procedures were performed, to give some indication of the physiologic effects of dynamite at the time of the headache. The results of routine blood counts and smears in all subjects were within normal limits. Urine analysis at the height of the headache revealed no glycosuria in any case, in spite of the fact that it has been reported that transient glycosuria occurs in such cases.³ Electrocardiograms were taken at the time of the headache, and in all cases essentially normal tracings were obtained. It was decided to determine accurately whether or not oral prostigmine bromide was desensitizing these men to histamine. The same subjects—those who had marked cutaneous reactions to histamine, as well as those who had been ingesting prostigmine—were given additional skin tests with 0.01 mg of histamine solution. In 90 per cent the severity of the local reaction was markedly reduced. Before oral desensitization with prostigmine bromide, the average

diameter of the wheal produced was 1.3 cm., after desensitization the average diameter was 0.45 cm., a significant reduction.

SUMMARY

The prime factor in the production of headache following contact with dynamite is its 20 per cent content of nitroglycerin, which can be absorbed through the unbroken skin to produce marked symptoms directly related to vasodilatation of the intracerebral vessels.

The psychogenic factor of fear did not play a role in the activation of the headache in subjects who were unaware of the nature of the patch test. It is entirely possible that some psychic element is active in subjects who realize the dangers associated with dynamite handling, but such a factor is not considered significant.

The intramuscular injection of 0.5 gm. of caffeine sodium benzoate followed by oral administration of 5 to 10 mg. of amphetamine sulfate greatly reduced and alleviated the symptoms of headache and within an hour gave lasting relief in over 95 per cent of the subjects.

The administration of 15 mg. of amphetamine sulfate daily for two or three days before exposure completely prevented the occurrence of the headache in all subjects, with minimal side effects.

Daily administration of oral prostigmine bromide in gradually increasing doses protected approxi-

mately 80 per cent of the subjects from the symptoms caused by nitroglycerin contact. It is quite reasonable to assume that desensitization results from a gradual liberation of minute quantities of acetylcholine that shock the intracerebral vessels to dilatation at regular intervals.

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TERMINAL ILEITIS WITH OBSTRUCTION AND ABSCESS COMPLICATING PREGNANCY

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IT IS the purpose of this paper to report and discuss a patient with cicatrizing ileitis, accompanied by obstruction and abscess, who was observed during the seventh month of pregnancy.

Regional ileitis is the most frequent chronic inflammatory disease of the small bowel and its mesentery. After Crohn¹ directed attention to this disease in 1932, sufficient operative cases had been reported by 1939 to allow Shapiro² to tabulate 519. Its occurrence in a severe form during pregnancy, however, has not been reported in the literature. Intestinal obstruction is also an unusual complication of pregnancy. Hansen,³ in 1941, noted 84 cases recorded in English. Williams⁴ mentions 2 cases in 30,000 deliveries. Slemons and Williams,⁵ in an analysis of types of intestinal obstruction recorded in the world literature, did not mention ileitis as a cause.

Surgical complications—particularly obstruction—in pregnancy should always be considered by the family physician, obstetrician and surgeon, the difficulty of recognizing such complications is well known. Pain is nearly always the prominent symptom. Blakely⁶ stated that the source of pain in pregnancy can be determined if a little care is taken in questioning and investigating the patient. Although pain frequently occurs in pregnancy, it should never be considered lightly, for it is occasionally the result of a serious pathologic state.

The management of acute surgical complications in pregnancy often presents a problem. Authorities are quite well agreed on certain aspects, on others, individual judgment is necessary, and no single rule can be laid down.

It is believed that these facts make the following case worthy of note.

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CASE REPORT

A 25-year-old primipara was admitted to an Army Forces regional hospital on April 12, 1945, because of abdominal pain and vomiting during the 7th month of pregnancy. Two months previously the patient had had an episode of diarrhea, vomiting and fever, for which she had been admitted to the obstetric service of this hospital. The symptoms subsided, and she was discharged after 3 hospital days, with a diagnosis of gastroenteritis. On the next evening she had a sudden, severe pain in the right lower quadrant that was steady and nonradiating and gradually decreased in severity. There was local tenderness and discomfort on motion and deep breathing. On the following day a physician stated that the pain was the result of pressure. The patient had subsequently had recurrent, shifting, sharp pain over the entire abdomen, gas pains and often steady pain in the right lower quadrant. The shifting pains were relieved by the passage of flatus or by bowel movements. The appetite was poor, and the patient vomited frequently. At times, when the colicky pains were severe, she could not

appeared to be emaciated. Except for the physical appearance and color, the positive findings were confined to the abdomen, which was enlarged, both from bowel distention and from the enlarged uterus extending 2 fingerbreadths above the umbilicus in keeping with the dates. The uterus lay largely to the left of the midline and during the examination contracted strongly at fairly regular intervals. The fetal heart was heard in the lower left quadrant, and a rate of 140 was noted. In the right lower quadrant a fixed, firm, extremely tender mass was observed close to the anterior iliac spine, approximately 6 by 8 cm in diameter. There was acute tenderness throughout the right side of the abdomen, but there was no referred rebound tenderness. No other organs or other masses could be felt. Peristalsis was intermittent and hyperactive. Rectal examination was not remarkable.

Examination of the blood revealed a red-cell count of 3,250,000, with a hemoglobin of 76 per cent, and a white-cell count of 10,800, with 76 per cent neutrophils. The icteric index was 15. The van den Bergh reaction was 0.5 mg direct, and the serum protein was 6.6 gm per 100 cc. The Rh factor was positive, and the blood Kahn reaction

TABLE 1 Supportive Therapy in a Case of Terminal Ileitis with Obstruction and Abscess

DATE	HOSPITAL COURSE	SUPPORTIVE THERAPY		
		WHOLE BLOOD*	5 PER CENT GLUCOSE†	AMIGEM AND 5 PER CENT GLUCOSE
4-12	Patient admitted to hospital	—	—	—
4-14		250	—	—
4-15		500	1000 (in normal saline)	—
4-16	Patient transferred to surgical service	—	—	—
4-17	Miller-Abbott tube inserted	500	—	650
4-18	Operation performed	1000	2000 (in normal saline)	1000
4-19		500	1000 (in distilled water)	1000
4-20		—	1000 (in normal saline) and 1000 (in distilled water)	1000
4-21	Miller-Abbott tube withdrawn	500	—	1000
4-27	Patient delivered	—	1000 (in distilled water)	1000
5-2	Onset of pelvic abscess	500	—	1000
5-3		500	1000 (in distilled water)	1000
5-4		—	—	1000
5-7	Abscess drained	—	—	—
6-7	Patient discharged	—	—	—

*One thousand cubic centimeters of whole blood is the equivalent of 146 calories or 35 gm of protein.

†One thousand cubic centimeters of 5 per cent glucose in normal saline solution or water is the equivalent of 200 calories, or 50 gm. of glucose.

‡One thousand cubic centimeters of Amigem with 5 per cent glucose is the equivalent of 400 calories or 50 gm of glucose and 50 gm of protein.

retain anything. She was admitted to another hospital 5 weeks later and was discharged after several days' observation, since it was stated that she was improved and presented no evidence of disease. The pain, vomiting and obstipation continued, however, until she re-entered this hospital.

Further questioning revealed that for several months in 1939 the patient considered herself to have colitis. The chief symptoms at that time were frequent loose stools with mucus, there was no blood, abdominal pain or vomiting. The patient continued with her schoolwork. Following this illness, except for a gradual loss of weight, the history was not remarkable until the onset of pregnancy, when difficulty in moving the bowels and ineffectual stools, with some tenesmus, were noted. These symptoms had increased in severity throughout pregnancy. There were also periods of diarrhea accompanied by marked weakness. The patient could remember no tarry or bloody stools. Prior to pregnancy, the appetite, digestion and bowel function had apparently been normal except at the time of the "colitis."

The past history revealed that the patient had never lived in the tropics. There had never been an injury or abdominal operation. The last period had occurred from September 26 to 29, 1944, making the expected date of confinement July 5. The patient had been married for 3 years. The weight in 1936 was 125 pounds, in 1942 115 pounds, in 1944, 102 pounds and at the time of final admission, 98 pounds. The family history was not contributory.

Physical examination on admission revealed a woman who appeared to be severely ill with a chronic disease. The temperature was 98.6°F, the pulse 102, and the respirations 18. The blood pressure was 112/70. There was a slight icteric tinge to the scleras, and the skin was pale and dry. The patient had obviously lost considerable weight and

negative. Examination of the urine was negative. The stools were negative for blood and ova.

Three days after admission a barium enema revealed an extensive lesion of the terminal ileum, with narrowing, fixation and distortion of 31 to 41 cm of bowel. The patient was given 2 whole-blood transfusions, the first being followed by a mild chill and a rise in temperature, — as well as other intensive supportive therapy (Table 1).

On April 17, the patient was transferred to the surgical service, where it was believed that there was an obstructive inflammatory lesion of the terminal ileum. X-ray films revealed passage of barium into what appeared to be a fistula through the bowel wall. The onset of severe pain 2 months before admission was regarded as representing a perforation, and an abscess was believed to be undoubtedly present between bowel loops. Terminal ileitis, tuberculosis, appendiceal abscess and cancer with perforation were considered, the first being the most probable diagnosis. It was believed that surgery was necessary because of the obstruction and the fact that the patient's poor condition precluded expectant treatment. Accordingly a Miller-Abbott tube was passed to relieve obstruction, to decrease the size of the small bowel and give more room at operation, and to relieve pressure on the suture line after operation. The patient was given 0.1 gm of Nembutal 1½ hours before operation, and 8 mg of morphine sulfate and 0.3 mg of scopolamine ½ hour later. Continuous spinal anesthesia was administered as follows: 100 mg of Metycaine at the start of and 25 mg during the operation. Whole blood was administered through a cannula in the ankle vein during operation.

At operation on April 18 an ileotransverse colostomy, with exclusion of the involved terminal ileum by transection of the ileum and closure of the distal end, was performed. A

right vertical abdominal incision was made lateral to the rectus, and the structures were divided in the direction of the wound. Exploration of the peritoneal cavity revealed a large inflammatory adherent mass involving the terminal ileum. In addition several loops of ileum proximal to the mass were densely adherent to each other and to the abdominal wall close to the iliac spine. There was considerable injection of the adjacent peritoneum, and exudate was present between the loops of intestine. Approximately 75 cm of terminal ileum was involved in a typical cicatrizing ileitis with undoubted fistula formation and abscess. The cecum, although somewhat adherent to the mass, was not involved. The ileum was divided between clamps well above the area of the lesion, and the distal end was turned in. The proximal end was anastomosed to the transverse colon, in an end-to-side manner, Young's clamps permitting a closed anastomosis. In the region of the bowel suture and in the wound 6 gm of sulfanilamide crystals were sprinkled. The abdomen was then closed without drainage.

There was considerable cyanosis postoperatively, the result undoubtedly of sulfanilamide in the abdomen. This rapidly cleared in 24 hours. There was marked improvement in the discomfort and pain in the abdomen. There was little nausea, the bowels moved by themselves on the 2nd postoperative day and freely thereafter. The Miller-Abbott tube was removed on the 3rd day. On the 5th day, however, the icterus index had risen to 55. The serum protein had fallen to 4.3 gm per 100 cc in spite of whole-blood transfusions, amino acids and forced protein intake. The urine contained a large amount of albumin and a great deal of bile. It was believed that the jaundice was the result of toxic hepatitis or of other factors, including chronic intestinal disease, acute infection, sulfanilamide and a toxic condition of pregnancy.

The intensive supportive care was continued with adequate fluid, protein and vitamin intake, crude liver extract and progesterone. The daily caloric intake was 2878, which was maintained by food (183 gm of carbohydrate, 131 gm of protein and 74 gm of fat) and by Casec (72 gm of carbohydrate, 158 gm of protein and 36 gm of fat). This was supplemented by intravenous injections, as shown in Table 1.

On the 10th postoperative day the patient went into active labor and delivered a living male infant weighing 3 pounds. The baby, however, survived only a few hours.

On the 14th day the patient complained of a sudden severe pain in the lower abdomen that began in the rectum and spread throughout the abdomen. Examination revealed evidence of spreading peritoneal irritation. The patient was apprehensive and in severe distress. The temperature rose to 101°F, and the pulse to 120, and the blood pressure fell to 100/60. It was apparent that some catastrophe had occurred. Perforation of an abscess and leakage at the suture line were considered. In view of the facts that since operation there had been no evidence of reaction about the anastomotic and transection sites and that the onset of this disturbance was in the pelvis, it was decided that pelvic peritonitis from the inflammatory mass was the likeliest diagnosis. Supportive treatment with blood and penicillin were begun. After several hours the patient improved and localization in the pelvis began to take place. Five days later a pelvic abscess was evacuated through the vagina. From this point on improvement was rapid. The abdominal incision healed by first intention. The patient gained strength rapidly and was discharged from the hospital on June 7.

At the time of a check-up examination on September 20 the patient weighed 110 pounds, felt extremely well, and had an excellent appetite. There was no indigestion or abdominal pain. The bowels moved 3 times daily, the first movement was formed and was followed in a few minutes by 2 small loose dejections. The gas pains, abdominal distress and bowel disturbance, which had been present during pregnancy, had completely disappeared. The periods were normal. Examination disclosed a marked improvement in appearance. Abdominal examination revealed a well healed scar. There was no tenderness or masses. Only slight thickening could be felt in the right iliac fossa. Pelvic examination was negative, as were blood and urine studies. X-ray films disclosed that irregularity and narrowing were still present in the excluded loop of terminal ileum, but repeated plates and fluoroscopy during passage of a barium meal showed no other bowel lesion. The anastomosis functioned well, and there was no tenderness, dilatation or further irregularity.

A final report from the patient on August 1, 1946, indicated that she remained well and weighed 117 pounds.

DISCUSSION

Surgery in ileitis is undertaken for patients with obstruction, fistula or abscess or who are unable to maintain weight and strength with reasonable freedom from symptoms under adequate medical management. Acute nonobstructive lesions in the early stages should not be disturbed, since the etiology is unknown and recurrence is frequent. The exclusion operation, as performed in the case presented above, yielded excellent results in the hands of Garlock and Crohn, who reported 164 cases followed for from two to fourteen years with the low operative mortality of 8.5 per cent.⁷ Resection in one or two stages has been advocated and practiced by many authorities, including Cave⁸ and Bockus.⁹ Marshall,⁹ at the Lahey Clinic, utilized obstructive resection with excellent results.

In the case reported, there was no choice regarding the type of surgical procedure. The involved loop was so completely fixed with inflammatory reaction that resection was completely ruled out. Following the exclusion operation improvement was so marked that further surgery was hardly advisable.

The management of abdominal surgical complications in pregnancy is always an extremely interesting and frequently a difficult problem. Phaneuf¹⁰ and De Lee¹¹ state that in cases in which operation is necessary the pregnancy should be disregarded. If delay is safe, postponement of operation is advisable. In cancer the questions of obstruction, operability and viability must be considered in each case. Occasionally, in intestinal obstruction, hysterectomy is essential, to disclose obstructive points hidden by the uterus.⁴ Cesarean section may be necessary in the true ileus of pregnancy.⁴

In the above case operation to relieve obstruction and to maintain life was urgently needed. It is evident from the pathologic state in the abdomen and the cachectic condition of the patient that an attempt to carry this patient on an expectant regime until viability was assured, with subsequent induction of labor, would have been fraught with grave danger to the mother. Certainly, maintenance of balance of nutrition would have been difficult or impossible for more than a few days without relief of obstruction, even with the aid of intestinal intubation. Accordingly, the pregnancy was ignored, and the short circuiting and exclusion procedure accomplished. Premature labor was almost a certainty, for vigorous contractions, indicating uterine irritability, were present from the time of hospital entry. Slemons and Williams⁵ and Phaneuf¹⁰ state that labor follows in a high percentage of such cases. In intestinal obstruction there is usually a

maternal mortality of 40 per cent and a fetal mortality of 65 per cent

This case illustrates the importance of abdominal pain in pregnancy, as well as the necessity of intensive and continued preoperative and postoperative care because of possible surgical complications and nutritional requirements. Incidental points of interest were the occurrence of jaundice and the rapid drop in serum protein values in the immediate postoperative course in spite of administration of large quantities of protein. The acute hepatitis undoubtedly interfered seriously with protein metabolism.

Continuous spinal anesthesia was probably of considerable value. It permitted a controlled anesthesia, produced by small quantities of drug at intervals, so that reactions could be avoided, excellent relaxation maintained, and time afforded for an accurate, gentle and meticulous procedure.

SUMMARY

A case of obstruction and abscess secondary to terminal ileitis in the seventh month of pregnancy is reported.

The unusual occurrence of severe obstructive ileitis in pregnancy is noted.

Certain aspects of the surgical management of the patient are briefly discussed.

79 Prospect Street

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MEDICAL PROGRESS

PRESENT CONCEPTS OF BENIGN BREAST DISEASE (Concluded)*

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CYSTS, HYPERPLASIAS AND PAPILLOMAS

The greatest difficulty in interpretation and classification is encountered in lesions that exhibit cysts, hyperplasias or papillomatous formation. The lesions frequently coexist with or are superimposed on the abnormalities described above. Thus it can be seen that the opportunity to designate some lesions as distinct entities is relatively rare. It is probable that the various changes are manifestations of the same syndrome, but the evidence is not conclusive. The lesions usually occur in women in the latter part of active sexual life. Unlike the syndromes described above, regression following the menopause appears to be less frequent, but this cannot be stated with certainty since observations are based entirely on patients who consult a physician. Cyclic swelling and objective symptoms other than the presence of isolated or diffuse lumpiness of the breast are conspicuously absent. The syndromes seem to occur more frequently in childless women, and coexistent pelvic disease is not unusual.⁸ The physical findings vary considerably and are difficult to define in many cases. For the purpose of clarification the lesions are described on the basis of the dominant histologic findings, even though other changes are found elsewhere in the breast.

Macroscopic Cysts

The solitary cyst or multiple cyst of similar origin and the so-called "blue dome" cyst of Bloodgood and others are easily distinguished. As Foote and Stewart¹³ pointed out, the lesions designated under this heading should be included only if they are isolated structures—that is, visible to the naked eye (1 mm. or more in size)—and distended with fluid and totally separate from the duct and lobule systems. It is further stressed that a diagnosis of microscopic cysts requires serial sections to prove complete isolation and loss of communication with the adjacent ducts or lobules. Lesions often appear cystic but are actually dilatation of the duct system or acini. Macroscopic cysts vary considerably in size, and if large enough, are tense to palpation. Epithelial linings are frequently absent, and hyperplasia is rarely found, even when the linings can be distinguished. Intracystic papillomas

and carcinomas are unusual.¹³ As a rule, lesions that appear to arise in cysts must be considered intraductal unless proved otherwise by serial section.

Hyperplasias

Epithelial hyperplasia in the duct systems and acini may occur with or without cysts. The degree of the proliferative process varies considerably in the same breast and may be palpated as a localized nodularity or as a diffuse process, usually of "doughy" consistence and with associated areas of irregular nodularity. Dilatation associated with blockage of the duct or lobule component by the proliferative lesion may resemble true cysts. Secretion, either serous or serosanguinous, may occur. These lesions resemble those originally described by Reclus.³¹

Papillomas

There is no sharp distinction between the simple hyperplasias and the more marked types resembling and tending to papillomatous formation. Frequently all stages of hyperplasia are seen in the same breast, and at times an apparent transition to papillomatous formation can be distinguished. For this reason many observers are of the opinion that these lesions are advanced stages of the simpler processes. Thus, a division based on the degree of hyperplasia must be arbitrary. Included under the designation of papillomas are the obvious and gross papillary lesions, with a definite stalk found in the larger duct systems, and microscopic lesions involving the smaller duct systems manifested by marked epithelial hyperplasia with papillomatous features and without obvious evidence of a stalk. Various degrees of papillomatous change are seen in the same breast, and may be associated with macroscopic cysts or duct or acinar dilatation or both.

The gross papilloma, which may be multiple, usually appears near the duct opening in the region of the areola and, although infrequently palpated, can sometimes be detected by transillumination and gross thickening of the proximal duct system involved and by mammography. Discharge from the involved duct is often seen and is usually serosanguinous in contrast to the fluid noted in other lesions. Occasionally the ducts containing gross papillomas can be identified by systematic palpation around the areola and by application of pressure at various points to elicit a discharge.

Microscopic papillomas are almost invariably found elsewhere in the breast in the presence of a

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oss papilloma Physical findings, although sometimes more pronounced, are essentially the same as those observed in breasts with only epithelial hyperplasia. The syndrome is consistent with that described by Schimmelbusch.²²

Other Lesions

Foote and Stewart¹³ have described and introduced new terms for several other lesions that appear to be distinctive. Although, as they point out, such terms may be undesirable, it is believed that such terminology should be encouraged, inasmuch as it stimulates interest and demands more specific interpretations of lesions that are frequently seen but poorly understood. These terms include the following:

Blunt duct adenosis In this manifestation, the duct ends abruptly near its distal portion without termination in lobules. The lumens are usually narrow, and the epithelial lining varies from simple hyperplasia to that resembling papillomas in the earlier stages. The advanced stages are characterized by dilatation and flattening of the epithelium. All degrees of change may be seen in a single breast. The process may exist as a single focus or as a palpable mass of nodularity, especially when lobules are absent and small cysts possibly arising as an end result of blunt duct adenosis are numerous.

Aprocrine epithelium Large, tall, cylindrical cells possessing relatively small nuclei and abundant, bright eosinophilic cytoplasm are characteristic of aprocrine epithelium, aggregates of which grossly present a discrete yellowish-brown appearance of slightly elevated, glistening areas, small in diameter, larger aggregates may be cystic as well.

Sclerosing adenosis This abnormality may be manifested as an early florid phase, characterized by epithelial proliferation, an intermediate phase and a late phase in which fibrous elements are dominant. It may appear as a grossly localized mass or more frequently as focal areas seen only on histologic examination. The lesions usually arise in terminal ducts or lobules.

Lobular alteration Primary and secondary types have been distinguished. For a complete discussion one is referred to the original study.¹³ In primary lobular alteration, as a rule, there is homogeneity of structures. The following three types, which are similar to adenofibrosis, are usually seen: a small number of lobules condensed with small, scanty acini and fibrous stroma often replaced by fat, an average number and size of lobules, with abundant, loose and edematous connective tissue and few but large and piled up epithelial components, and an irregular—that is, heterogeneous—lobule pattern that in some cases exhibits epithelial activity and in others appears to be undergoing regression,

with evidence of atrophy and cystic formation. In secondary lobular alteration, lobules adjacent to a mass—such as cysts, fibroadenomas and cancer—exhibit interlobular edema, changes in contour and size, epithelial components and round-cell infiltration, as the primary lesions progress or persist, however, all degrees of change are noted until the lobules are obliterated, edema disappears and round-cell infiltration is predominant.

Objective evidences of these newly designated microscopic lesions are difficult to define. By correlation of clinical and histologic observations, however, it is likely that they will be clarified.

It is necessary to emphasize again that the lesions discussed under the term “chronic cystic mastitis” are not necessarily separate entities, but may coexist in any combination to complete the general picture.

RELATION OF BENIGN LESIONS TO CARCINOMA

This problem has been discussed elsewhere,^{3, 13, 23-30} but the increasing statistical and histologic observations warrant additional evaluation. It is becoming increasingly apparent that certain lesions are apt to be associated with or to precede cancer of the breast whereas others are equivocal or may be of no significance. The more thorough studies indicate that adenofibrosis,²⁹ fibroadenomas^{13, 29} and macroscopic cysts¹³ are less often seen in conjunction with cancer of the breast. Other lesions included under chronic cystic mastitis are more difficult to evaluate. These manifestations, which have a greater tendency to be associated with carcinoma, are marked epithelial hyperplasia,²⁹ papillomatosis^{13, 29} and, possibly, blunt duct adenosis.¹³ As pointed out by several observers, the papillomatous lesions, especially when atypical, precede or coexist more frequently with carcinoma.^{13, 29} In some cases transition from the benign state to the neoplastic process can be demonstrated.¹³ An appraisal of the situation with a broad point of view indicates that any of the abnormalities alluded to—with the possible exception of fibroadenoma—may precede or coexist with malignant change in the breast. Some are obviously of a special significance, but as yet they cannot be defined with certainty. For the moment the question is still open, but it is expected that studies will continue to elucidate this fundamental problem.

BENIGN BREAST DISEASE IN THE MALE

As in the female, certain benign disease of the male breast is erroneously designated mastitis. The term mastitis should be used only for specific inflammatory processes that are rare and apparently bear no relation to the lesions usually seen in the male. Gynecomastia is also used by some observers as a general term to describe the common forms of benign breast disease in the male, but it should be reserved for a special group as pointed out below. For these reasons, the term “mammoplasia” is

suggested to describe the benign noninflammatory processes, which are transient in character and as such are distinguished from gynecomastia. It is realized that introduction of another term into an already confused field may be undesirable, but it is believed justifiable in view of advances made in the concepts of breast disease in general.

Adolescent or Pubertal Mammoplastia

This condition, which in the male is akin to the changes seen normally at the onset of breast development in the female, usually appears between the twelfth and seventeenth years and is characterized by the presence of a well defined, freely movable, discoid mass beneath and closely associated with the areola. The mass varies in size from less than 1 to 5 cm., but as a rule is 2 or 3 cm. The nipple and areola may also be increased in size. The process is usually unilateral at the onset, but may affect both breasts, simultaneously or successively.³³ It occurs more frequently than is generally recognized. Jung and Shafton⁶ in approximately a thousand examinations found that it was an integral part of the process of puberty. It is not seen oftener because of the frequently transient character of the process, which may arise and regress within even a month. Histologic examination reveals lengthening and hypertrophy of the ducts, with an increase in periductal connective tissue. Lobule formation is usually absent. In a small percentage of cases this lesion persists and may then be correctly called gynecomastia. A process similar to adolescent mammoplastia is seen in postadolescent males. A number of cases were reported in soldiers in World War II. Few, if any, had a history of previous breast trouble so that the process may well be similar to that noted in the adolescent.

Gynecomastia

In gynecomastia the contour and elements of the breast approach those of the normal woman. As stated above the abnormality may represent a persistence of the adolescent type or may arise spontaneously in the adult or in the presence of associated diseases. It may be unilateral or bilateral. Histologically, in addition to the changes described above, there may be hyperplasia of the duct epithelium, dilatation of the ducts and occasional secretion. The presence of acini and lobules is rare. The main differences from the other types of benign breast disease in the male are the persistence and the physical characteristics.

Senescent Mammoplastia

After the age of forty-five years, but particularly after sixty, changes resembling those seen at puberty are frequently encountered. Some, of course, occur earlier. The disease behaves in a fashion similar to that seen in the youth, but spontaneous regression is not so frequent.

Etiologic Factors

There are no obvious associated abnormalities in the large majority of these cases. Adolescent and senescent mammoplastia, as noted, occur at the extremes of active sexual life. It is possible, therefore, that at these periods there is a temporary hormonal imbalance. Both mammoplastia and gynecomastia, however, occur in association with other diseases and in such cases possible etiologic factors are apparent. These may be described as follows.

Atrophy of the testicle following orchitis or injury

The spermatic tubules are frequently atrophic and the atrophy thus accompanied by a relative or actual increase in the interstitial cells. Since these cells are supposedly the site of origin of androgens, it is possible that they are responsible for the change in the breast.

Neoplasms of the testes Mammoplastia and gynecomastia are sometimes associated with tumors of the testes, particularly chorioepithelioma. Gilbert³⁴ is of the opinion that the breast lesions are of two types — a "physiologic," resembling the usual mammoplastia in males and not necessarily related directly to the tumor of the testes, and a "choriogenic," most frequently related to the chorioepithelioma and resembling the female breast in its histologic characteristics, especially during pregnancy. The pituitary gland in cases with choriogenic gynecomastia shows changes that are also seen in pregnancy. In contrast to the physiologic type, these lesions may be caused by the hormones secreted by the tumor itself. Several cases of gynecomastia have also been associated with interstitial-cell tumors of the testes.³⁵ The nature of the stimulus in these cases is not clear, for although one would expect the androgens to be in excess, 1 patient had loss of libido suggesting destruction of testicular function and failure of the tumor to secrete a hormone to maintain such a function.

Functioning tumors of adrenal cortex These tumors may produce feminization, in contrast to the usual masculinizing syndrome seen in females and prepubertal males.^{36, 37} The syndrome is characterized by mammary enlargement, regression of secondary sex characters and atrophy of the testes. Since estrogens as well as androgens have been recovered from the adrenal gland and because elevated excretion levels of both these substances are frequently found in patients with adrenocortical tumors, a hormonal cause seems evident, especially since removal of the tumor is followed by regression of the breast lesion.

*Hypophyseal adenoma*³⁸ These lesions may give rise to atypical pituitary secretion affecting the breast directly or indirectly as a result of stimulation of the peripheral endocrine organs.

Cirrhosis of liver Breast changes associated with cirrhosis are sometimes encountered.³⁹ The

patients often show testicular atrophy. It is conceivable that the breast lesions may be caused by faulty metabolism of the hormones as a result of liver cirrhosis, since the liver is intimately concerned with such a metabolism. An alternative possibility is a loss of testicular function.

Syndrome of unknown cause A syndrome characterized by aspermatogenesis, testicular atrophy and gynecomastia without known cause has been reported by Klinefelter and co-workers.⁴⁰ The testicular changes resembled those seen after orchitis or injury, and may possibly fall into the same category.

Other conditions The mechanism involved in the production of mammoplasia in patients with thyrotoxicosis,⁴¹ leukemia and pulmonary carcinoma, as well as in soldiers with malnutrition or debilitating diseases,⁴² is not clear. It seems, however, that in these diseases there is also a disturbance of the metabolism of the hormones.

Hormonal induction Mammoplasia of a transient character develops in eunuchs following the injection of testosterone.⁴³⁻⁴⁴ Such treatment is followed by an increased excretion of estrogens in the urine and suggests, therefore, a metabolism or conversion of the androgens to estrogenic substances.⁴⁵⁻⁴⁷ This may be characteristic for the eunuch, since such changes after administration of androgens to a normal person are exceedingly rare. As would be expected the administration of estrogens to the male for various causes — especially carcinomas of the prostate gland — results in mammary hypertrophy.⁴⁸⁻⁵¹ The nipples and areola enlarge, and in some cases there is marked epithelial proliferation and acinar formation. Interestingly enough, I have observed unilateral or asymmetrical response after estrogen therapy. Such a finding is consistent with the concept of differential tissue sensitivity. Removal of the stimulus results in relatively rapid regression of the process. Excretion studies of gonadotropic and sex hormones in the urine have been fully described elsewhere.³

Benign breast disease in the male seems to be associated with an endocrine imbalance, either as a result of sexual metamorphosis or of an associated abnormality or tumor. Since the changes normally produced by the various hormones are not identical, clarification may come when a careful correlation is made between the histologic appearance of the breast and a known activating agent. A common denominator may be found in the so-called "mammogenic hormones,"⁵² which may be activated by either estrogens or androgens. Hence, similar lesions could be produced by these different hormones. Most of the available data point to the estrogens as an important factor. Changes induced in the breast by the administration of estrogens are frequently seen, but except in the eunuch testosterone seldom pro-

duces obvious breast abnormalities. Moreover, testosterone has been used with success in the treatment of the more transient types of mammoplasia. These paradoxical findings may possibly be explained by a difference in the metabolism of the hormones as a result of disease or variation in the endocrine status.

DISCUSSION

The available clinical and experimental information emphasizes the significance of the endocrine system in the development and growth of the mammary gland. The ovary and hypophysis are especially important, for without one or the other breast development does not occur or ceases entirely. Furthermore, removal of these organs leads to regressive changes in the fully developed breast. Thus, it has been contended that disease of the breast is definitely related to or caused by alterations of function or secretion of certain glands of internal secretion. Factual data, for such a thesis, have been reviewed elsewhere.² A general discussion of the possibilities involved seems necessary, however, since certain factors are common to all types of breast disease.

Factors other than endocrine must be considered in the development of breast disease. Chief among these are heredity, race, color and constitutional type, which are frequently interrelated but may be individually of special significance. Although the evidence to support these possibilities is far from conclusive, one may justifiably speculate on them. Physiologic status, endocrine metabolism and secretion and susceptibility to the disease may depend to a considerable degree on these fundamental backgrounds. These basic states in some measure may thus determine the type and degree of response of the organism to normal or superimposed stimuli. This would help to explain the variety of changes in the breast that have been attributed to the same agent, such as estrogens.

The stage of life and state of the breast when abnormalities appear may also determine the type and degree of response to a given stimulus. It has been shown that the histologic structure and clinical manifestations of diseases that arise during various age periods vary considerably. Moreover, the degree of development and structure of the breast may differ regardless of age as a result of variations in physiologic status. Dieckmann⁵ has shown that the extent of development of the breast, particularly at puberty, is subject to wide variation among different persons. Previous pregnancies and normal and abnormal lactation account for breast changes not encountered in the virgin female. Other processes, such as inflammatory disease, may likewise alter the state of the breast. Thus, the breast may exhibit wide varieties of histologic structure under different conditions, and these dissimilar substrates may therefore vary considerably in their response to a

single stimulus and may determine to some degree the abnormal changes that subsequently appear

Foremost among the probable stimuli responsible for breast disease are those of the endocrine and nervous systems. The hormones that have been the subject of the most intensive study are the estrogens. Nevertheless, the possibilities suggested by investigations may apply to other hormones as well. How may estrogens produce these atypical states? Several possible modes of action seem tenable. Physiologic amounts of the hormone may act on tissue that is more sensitive than normal. This susceptibility may be related to the metabolic status of the host, to special characteristics of the cells, or to a change in the breast as a result of the activity of other agents. It has been demonstrated that estrogens are destroyed by the liver. Normal quantities of the hormone may be secreted, but because of defective function of the liver, abnormal quantities may be released to the tissues. Excessive quantities of the hormone may be responsible, but, except in cancer-susceptible animals, the effects are limited. Atypical hormones with carcinogenic activity may be produced. This is possible since the steroid hormones are closely allied to several of the known synthetic carcinogens. It is conceivable that the formation of carcinogenic agents from hormones may occur as a result of a faulty metabolism due to a change in the physiologic state of the host. Lack of a hormone, which normally stimulates the breast, may lead to degenerative or regressive changes that may then allow other agents to act.

As has been pointed out, the nervous system may also be involved. The action may be direct, but it is more probable that such stimuli exert their effect by causing excesses or alterations of hormonal secretion. Furthermore, the close interrelation of the various endocrine organs suggests that disturbance of one organ could affect the function of the others. Because of the possible methods of action or alterations of hormonal secretion, there is still lack of conclusive evidence to justify the acceptance of any one factor.

As suggested above, the state of the breast at the time that an abnormal stimulation is superimposed is probably of some importance. Infantile and virginal hypertrophy, early ripening, adenofibrosis, fibroadenomas in the female and gynecomastia and mammoplasia in the male are remarkably similar in histologic appearance and in their resemblance to changes usually seen in the normal adolescent female. It is conceivable, therefore, that they may be due to the same etiologic agent, possibly the hormones. Lewis and Geschickter²¹ emphasized this similarity in virginal hypertrophy, gynecomastia and fibroadenoma, and there is fairly good evidence to support such an opinion. The different forms of disease classified under the present accepted designation of "chronic cystic mastitis" also basically

resemble each other, in spite of considerable variation in the individual case.

It has repeatedly been stressed that lesions described above as possible entities may coexist in the same breast. This suggests that each type may represent a later stage of or may be superimposed on the same basic abnormality. The changes may represent manifestations of quiescence or stimulation as indicated by involutions or proliferations that in part may have occurred prior to the time of examination. Thus, this point of view reverts to the thesis that localized areas of the specific tissue are unusually sensitive to a stimulus. It is my opinion that this sensitivity is a major determining factor in the production of the heterogeneous groups of lesions described.

In almost all types of breast disease—from the simple infantile hypertrophy to complex breast cancer—there is a suggestion of some dysfunction of the endocrine system in many cases. Nevertheless, it can be stated that evidence is insufficient to support the thesis that the hormones themselves are directly responsible for the production of benign and malignant lesions. It is possible, however, that they may be exciting factors or may prepare a suitable substrate and thus contribute to the initiation and production of the varieties of breast disease.

As a result of increasing knowledge and clarification of lesions of the breast, concepts have changed in the last decade regarding management of benign disease. A solitary mass or a localized nodularity, as has been repeatedly emphasized in all teachings on breast disease, must be investigated surgically, since it is often impossible to distinguish between clinically benign lesions and early cancer. Obviously, radical mastectomy must be performed if the lesion proves to be cancer. The removal of a localized benign process may be all that is necessary, particularly in young women. Thereafter, systematic observation should be instituted.

Benign lesions except for the so-called "precancerous hyperplasias" are of significance so far as they cause annoying symptoms or exert an unfavorable psychologic effect on the patient. It is the responsibility of the physician to decide on the proper management in the individual case. This demands, therefore, an objective view based on a broad comprehension of breast disease. Since many of the lesions are diffuse one is faced with the choice of conservative management or a simple mastectomy, if the indications warrant it, as a preventive measure against cancer. The majority of benign diffuse processes frequently involve both breasts, and it therefore seems illogical to perform unilateral simple mastectomy as a prophylaxis against cancer. Warren²² states that if an excised focus of chronic cystic mastitis shows evidence of definite precancerous hyperplasia, a simple mastectomy should be performed. He believes, however, that there is not sufficient risk of subsequent develop-

ent of carcinoma in the remaining breast to warrant or justify bilateral mastectomy as a rule. It is by conviction that simple mastectomy is performed so frequently for benign lesions of the breast.

Conservative management and reassurance is all that is necessary in handling the syndromes of adenosis and nonpuerperal secretion, in the absence of a localized mass. So far as cystic disease is concerned, the process is often diffuse. It is not unusual to find additional cysts arising after a solitary lesion has been removed surgically. The surgeon is therefore faced with the problem of another or repeated excisions, simple mastectomy or conservative management.

Solitary large cysts may be aspirated with considerable safety, since the possibility of cancer within the lesions described is relatively remote. As a rule, however, these lesions recur, and surgical intervention is necessary for eradication. If multiple cysts are found and the diagnosis is verified by aspiration or local excision of a typical lesion, careful observation in a majority of cases will accomplish the same effect in the end as a radical procedure. In young women particularly the psychologic effect of simple mastectomy may be profound, in older women there is less emotional reaction to the procedure.

When one is faced with the more complex structures—particularly those of precancerous hyperplasia or papillomatous change—the problem becomes increasingly difficult. In the single gross papilloma, excision of the entire duct system may be all that is necessary. The gross lesions may be multiple, however, so that every effort should be made to identify them. If the papillomatous process is diffuse or atypical or if precancerous hyperplasias exist, it is probably wiser to carry out simple mastectomy as a prophylactic measure because of apparently close association with cancer.

CONCLUSIONS

The endocrine organs and their secretions are necessary for normal growth, development and maintenance of the mammary gland. As such, they are indirectly responsible for breast disease, since they provide the tissue in which the lesions arise.

Factors such as heredity, constitution, race, color and physiologic state of the patient must also be considered causes of breast disease.

The state of the breast at the time of onset of disease seems to be an important factor in the type

of lesion seen. A single stimulus may thus produce a variety of apparently different lesions.

Localized tissue susceptibility may account for an unusual response to an apparent normal stimulus.

Endocrine dysfunction is frequently associated with and may be responsible for certain benign lesions, but there is no absolute proof that it is the only or direct etiologic factor.

A number of histologic lesions classified under the general term of chronic cystic mastitis may be distinct entities, but they frequently coexist in the same breast.

A revised classification of breast lesions and a recognition of these as distinct entities is essential to a better understanding of etiologic factors and to intelligent management of the individual case.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 32411

PRESENTATION OF CASE

A sixty-nine-year-old unemployed woman, formerly a practical nurse, entered the hospital because of palpitation.

The patient had been in good health until two and a half years before admission, when she first noted shortness of breath and palpitation after mild exertion. From then on exertional dyspnea progressed steadily until she was unable to do more than walk about her room without precipitating an attack. During the same interval, orthopnea developed and there were occasional attacks of nocturnal dyspnea, usually of no more than fifteen minutes' duration. Palpitation was always a prominent symptom, occurring at first only following exertion but later during bed rest. For six months there had been a constant, increasing coarse tremor of both hands and arms. Slight numbness and tingling of the fingers had appeared during the previous two months. Nocturia (two or three times) and frequency during the day appeared in the course of the illness. There was never any swelling of the hands, face, abdomen or ankles, or any precordial pain, oppression or convulsive seizures. Three days before admission the patient fainted, falling across the bed. Several minutes after she regained consciousness there was a spontaneous brisk nosebleed, which lasted several minutes. She noticed no visual changes or muscular weakness on recovery. She had never had hypertension. During the two and a half years of illness there had been progressive anorexia, accompanied by a 55-pound weight loss. Muscular weakness was a prominent symptom.

For three months after the onset of the symptoms the patient had been given digitalis by a physician but had subsequently received none. For two years she had received weekly injections of liver and many iron tablets. Three months before admission 20 drops of iodine solution was administered three times daily, and the patient thought that she felt stronger for a time.

As a child the patient had had aches first in one knee and then in the other that lasted several days. The joints were not swollen, and she was not put to bed.

Physical examination revealed a thin, pale woman exhibiting a marked coarse tremor of the hands and lips. The face bore a masklike expression. The skin was dry and warm. The arms and legs were wasted and weak. There was slight exophthalmos, lid lag and infrequent blinking. The thyroid gland was slightly enlarged and nodular. A Grade III systolic and a harsh mid-diastolic murmur were heard at the apex, and there was a Grade II or III systolic murmur in the aortic area. Flatness, decreased breath sounds and decreased tactile fremitus were elicited at the left lung base. The liver edge was palpable three fingerbreadths below the costal margin. The tremor of the hands was more marked on intention. Pelvic examination revealed tenderness in both vaults, no masses were palpable. There was tenderness over the lumbar spine and sacrum.

The temperature was 98.0°F, the pulse 95, and the respirations 20. The blood pressure was 110 systolic, 58 diastolic.

Examination of the blood showed a red-cell count of 1,890,000, with a hemoglobin of 67 gm, and a white-cell count of 11,800, with 94 per cent neutrophils. The hematocrit was 19 per cent. The non-protein nitrogen was 140 mg, the total protein 7.2 gm, with a normal albumin-globulin ratio, the blood sugar 108 mg, and the calcium 9.6 mg per 100 cc. The basal metabolic rate was +11 per cent. The specific gravity of the urine was 1.006, and there was a + albumin reaction, the sediment contained 3 white cells and 1 epithelial cell per high-power field. A stool was brown and gave a ++++ guaiac test.

On x-ray examination the heart appeared enlarged on both sides and also in the anteroposterior diameter. The aorta was extensively calcified from the arch to the iliac arteries. The left pleural cavity contained a moderate amount of fluid, and there was a small amount on the right. An electrocardiogram showed inverted T₁, T_{CR1}, and T_{CR2}, prominent S₂, upright T₂, T₃, and T_{CR3}, and depressed ST_{CR1} and ST_{CR2}. The rhythm was normal.

The patient was slightly short of breath, slightly orthopneic and extremely weak but had no specific complaints. Barium studies of the upper gastrointestinal tract showed the esophagus displaced to the right and posteriorly, apparently by the left auricle (Fig. 1). The stomach and duodenum were normal except for a pressure defect produced in the latter by the gall bladder. The severe anemia did not improve. White cells up to 20 per high-power field appeared in the urine, which was otherwise unchanged.

On the fourth hospital day the patient suddenly sat up in bed and expired.

DIFFERENTIAL DIAGNOSIS

DR. RULON W. RAWSON: May we see the x-ray films?

DR. JAMES R. LINGLEY The heart shows marked generalized enlargement, without characteristic configuration. The lung fields are clear, but there is fluid at both bases, more marked on the left than on the right. The esophagus is displaced, as described in the record, apparently by this enlarged left auricle. I think that that goes along with the general cardiac enlargement. On this lateral view there is also a ring of calcification in the heart, which corre-

thought to be an enlarged left auricle, makes the diagnosis almost certain. The aortic systolic murmur can be explained by rheumatic heart disease, but can likewise be explained by arteriosclerosis and the calcified aorta that Dr. Lingley has shown us.

Dr. Bland tells me that the electrocardiographic changes are consistent with coronary heart disease and some old infarction but states also that it could be explained on the basis of anemia. The finding of



FIGURE 1 Lateral Chest Film, Showing Generalized Aortic Calcification, Calcification of Mitral Annulus and Pressure Displacement of Esophagus by Left Auricle

sponds to the annulus of the mitral valve. There is an extreme degree of calcification in the aorta, apparently it extends the entire length from the heart to the bifurcation.

DR. RAWSON It is impossible for me to ascribe this entire picture to one disease entity. The diagnosis of old rheumatic heart disease seems a sure bet. The history of the joint pains in childhood suggests it, and the Grade III systolic and the mid-diastolic murmurs at the apex are also suggestive of that. The x-ray finding of enlargement of the heart on both sides in the anteroposterior diameter, with displacement of the esophagus to the right by what was

fluid in the chest can be adequately accounted for on the basis of cardiac failure, as can the enlargement of the liver, although enlargement of the liver could also be explained by some other diagnostic possibilities, which I shall discuss.

In view of the weight loss, the tremor, the palpitation, the lid lag, the exophthalmos, the warm skin and the symptomatic improvement following the administration of iodine one has to think of Graves's disease. The weight loss can be explained on the basis of anorexia. The tremor was a coarse one. As a rule the tremor in Graves's disease is fine and rapid. Frequently in older people we do see a

coarse tremor, which is rapid, however. There is no statement whether or not this tremor was rapid. I should prefer to attribute it to weakness. The palpitation could also be explained on the basis of thyrotoxicosis, but I think that it is adequately accounted for on the basis of heart disease and the anemia. Enlarged liver does occur with long untreated Graves's disease, but again is adequately explained on the basis of heart failure. The eye signs, the goiter and the subjective improvement on the administration of iodine are strongly suggestive of Graves's disease. The basal metabolic rate, however, was only +11 per cent, which is quite low for a patient this ill with thyrotoxicosis, especially in the presence of heart failure. Usually patients with heart failure have elevated basal metabolic rates, whether or not they have thyroid disease. It is of interest that a number of years ago in an analysis of patients in this hospital who had heart disease and on whom total thyroidectomies were done, it was found that frequently when they returned to the hospital or clinic in a state of decompensation the basal metabolic rate was elevated as high as +20 to +25 per cent, and that when compensation was restored and the fluid removed, the basal metabolic rate fell to -20 per cent or lower. So I am skeptical of the diagnosis of Graves's disease with a basal metabolic rate of only +11 per cent, especially with cardiac decompensation. We have seen a few patients, however, who entered the hospital with thyroid storm and who were so debilitated that had we been able to determine the basal metabolic rates, it is possible that they would have been found low. It should be pointed out that neither the cardiac failure, the decompensation nor the hyperthyroidism can account for this degree of anemia. Also, it is important to recognize that the white-cell count of 11,800, with 94 per cent neutrophils, is not a classic picture for Graves's disease. Usually there are leukopenia and lymphocytosis.

The anemia was hyperchromic. The color index was 1.25, with a mean corpuscular volume of 1, and therefore one should consider the diagnosis of pernicious anemia. The anorexia for two and a half years and the ++++ guaiac reaction in the stool make one look at the gastrointestinal tract as a source of blood loss, and as a cause of this particular type of blood picture. A malignant growth in the cecum or stomach could produce this type of blood picture. Since the radiologist found no evidence of disease in the examination of the stomach one is likelier to look at the cecum for the primary lesion. I think that the last case I discussed before this group, however, was a case of carcinoma of the stomach with a positive guaiac reaction in which the radiologist considered the examination of the stomach to be negative. The negative x-ray examination certainly does not rule out cancer of the stomach. The pressure defect in the duodenum was said to have been due to the gall bladder. One might

also suggest that this was a peritoneal lymph node, and therefore one should consider the possibility of lymphoma, probably of the abdominal type. The patient had no fever, however, which speaks against Hodgkin's sarcoma or abdominal lymphoma. A lymphosarcoma of the stomach or bowel is a possibility.

I think that the fainting episode three days before admission can be accounted for on the basis of a large gastrointestinal hemorrhage. Since the total blood protein of 7.2 gm per 100 cc following what I think was a hemorrhage seems rather high, one should list plasma-cell myeloma as a possibility. The nonprotein nitrogen of 140 mg per 100 cc merits comment. I think that it can be explained on the basis of cardiac failure, gastrointestinal bleeding and arteriosclerosis. The sudden death could have been due to embolism or a massive gastric hemorrhage.

My first diagnosis, therefore, is rheumatic heart disease, with mitral stenosis, aortic stenosis, arteriosclerosis and cardiac decompensation. I shall list as my second diagnosis cancer in the gastrointestinal tract, probably carcinoma of the cecum.

DR. TRACY B. MALLORY: The level of the nonprotein nitrogen apparently does not bother you, Dr. Rawson.

DR. RAWSON: The patient may have had an old nephritis. The arteriosclerosis probably involved the kidney, however. Also, she quite likely was in shock, which would explain in part the elevated blood nonprotein nitrogen.

DR. WALTER BAUER: Certain findings suggest the possibility of multiple myeloma, but there is nothing that you can "hang your hat on" with certainty.

CLINICAL DIAGNOSES

Uremia
Anemia
Generalized arteriosclerosis
Coronary heart disease
Old rheumatic heart disease, with mitral stenosis
Chronic nephritis
Carcinoma of bowel?

DR. RAWSON'S DIAGNOSES

Rheumatic heart disease, with arteriosclerosis, mitral and aortic stenosis and cardiac decompensation
Carcinoma of cecum

ANATOMICAL DIAGNOSES

Acute rheumatic myocarditis
Calcification of aortic and mitral valves and of annuli of aortic, mitral and tricuspid valves.
Arteriosclerosis, with extreme calcification of aorta and coronary arteries
Chronic glomerulonephritis
Adenocarcinoma of cecum
Colloid adenoma of thyroid gland
Reduplication cyst of duodenum

PATHOLOGICAL DISCUSSION

DR. MALLORY We discovered a wide variety of anatomical findings, most of which Dr. Rawson has predicted correctly. There was a severe grade of heart disease, which was rather peculiar in character. As Dr. Lingley pointed out, in this x-ray film, there was an extreme grade of calcification of the annulus of the mitral valve, and almost equal calcification of the aortic ring. In neither valve was there any interadherence of the cusps or any shortening of the chordae tendineae, so that the gross picture was not characteristic of a chronic rheumatic endocarditis. There even was calcification of the annulus of the tricuspid, which is rare. Considerably to our surprise on microscopic examination the myocardium was full of fresh Aschoff bodies. We can say without doubt that the patient had a terminal acute rheumatic infection, since that is a pathognomonic lesion. There was a carcinoma of the cecum, which was ulcerated. The pressure defect on the duodenum was caused by a cyst, which I believe was congenital in origin, lying between the cecum and the gall bladder. It was lined with an enteric membrane and represented one of those duplications of the intestinal tract often seen in children but rarely in adults. Evidently it had never caused any trouble.

DR. BAUER How large was it?

DR. MALLORY About 4 or 5 cm. in diameter.

There was also an extreme grade of arteriosclerosis in the entire aorta, as seen in the x-ray film. The aorta was calcified from the arch down to the iliac artery. There was likewise marked calcification in the coronary arteries. The thyroid gland showed only an old colloid adenoma. The kidneys were small, weighing 100 gm., and were finely granular and pale—the gross appearance usually associated with chronic glomerulonephritis. On microscopic section an active process was present. There had evidently been extensive destruction of the cortex, and we found an unusually marked sclerosis of the large and intermediate arteries, but little sclerosis of the arterioles, such as one sees in chronic nephrosclerosis. It seems astonishing to me that such a severe renal lesion had occurred without any record of hypertension. You may take your choice in attributing the anemia to the carcinoma or to the nephritis.

DR. RAWSON The patient was in shock.

DR. MALLORY But she had been under competent medical observation for three years and had never shown an elevated blood pressure in that period.

DR. RAWSON Do you think that she had previously had early rheumatic lesions in the heart?

DR. MALLORY I confess that I do not know how to interpret these calcareous lesions of the heart. The majority opinion is that they are rheumatic in origin. There has always been a small minority questioning that assumption, and I have been in

the minority. In many of these cases the most frequent features of rheumatic involvement are missing. For example, in this case, there was no involvement of the valves and no thickening or shortening of the chordae, the two most reliable stigmas of old rheumatic involvement of the mitral valve. But I must grant the terminal rheumatic myocarditis.

CASE 32412

PRESENTATION OF CASE

A forty-five-year-old screen painter entered the hospital because of swelling of the abdomen.

The patient had apparently been well until ten months before entry, when he became aware of increasing fatigue and exertional dyspnea. Five months later he noticed that he "looked thin" in the face and arms, and in another month a black bowel movement occurred. Six weeks before entry the abdomen gradually began to swell, and he caught a "cold," with a persistent hacking cough, occasionally productive of pinkish sputum. He also noticed that the stools were becoming light yellow and that his appetite was diminishing. Nevertheless he continued to work.

Twenty-five years before entry the patient had acquired a chancre on the penis, for which he received antisyphilitic therapy irregularly for the next twenty years. Fourteen years before entry, after a three-month period of treatment, he had become jaundiced but had recovered while still receiving intravenous injections. He admitted drinking two or three glasses of whiskey a day for many years. For two years before entry he had had occasional epistaxes and bleeding gums, with some increase in bleeding tendency during the last two months before admission.

Physical examination revealed a poorly nourished man with a thin face and extremities and a protuberant abdomen. Numerous spider angiomas were scattered over the arms and back. There were dullness and a few medium rales at both lung bases. The heart was normal except for a faint, blowing systolic murmur heard best in the aortic area. The abdomen showed a prominent venous pattern and obvious ascites. The liver edge was felt two or three fingerbreadths below the costal margin. There were scattered hematomas over the legs but no ankle edema. The deep-tendon reflexes were normal.

The temperature, pulse and respirations were normal. The blood pressure was 132 systolic, 95 diastolic.

Examination of the blood showed a red-cell count of 4,400,000, with 75 per cent hemoglobin, and a white-cell count of 4700, with 63 per cent neutrophils and 30 per cent lymphocytes. The total protein was 7.8 gm. per 100 cc., with an albumin-globulin ratio of 0.56. The van den Bergh reaction was 10 mg. direct and 18 mg. total. The pro-

thrombin time was normal. The cholesterol was 327 mg (normal, 150 to 230 mg) and the phosphorus 3.3 mg per 100 cc, the vitamin A 10 units (normal, 40 to 100 units) and the carotenoids 130 units per 100 cc (normal, 100 to 300 units) and the alkaline phosphatase 91 Bodansky units. A cephalin-flocculation test was + in twenty-four hours and ++++ in forty-eight hours. Blood Hinton and Wassermann tests were positive. The urine was normal. A bromsulfalein test (5 mg per kilogram of body weight) showed 36 per cent retention of the dye.

X-ray examination of the chest revealed several linear areas of segmented atelectasis in the left lower lung field and moderate collapse of the right middle lobe. The diaphragm showed adequate excursion, except for somewhat limited motion of the medial portion of the left dome. A gastrointestinal series disclosed extensive varicosities in the lower esophagus.

The patient was placed on a high-calorie, high-protein, high-vitamin, low-fat and low-salt diet, but no clinical improvement was noted. He complained of increased abdominal distention, as well as pain in the right chest posteriorly that was brought on by coughing or by raising the right arm. He also had several epistaxes. Mercupurin and ammonium chloride failed to control the ascites. On the tenth hospital day a paracentesis was performed, and 5500 cc of straw-colored fluid removed. Repeated blood studies on the fifteenth hospital day revealed a total protein of 6.73 gm per 100 cc, with an albumin-globulin ratio of 2.7. The van den Bergh reaction was 1.2 mg direct and 1.4 mg total. The prothrombin time was 25 seconds, with a normal control of 20 seconds. The cholesterol was 208 and the phosphorus 6.8 mg per 100 cc, the vitamin A 50 and the carotenoids 40 units per 100 cc and the alkaline phosphatase 68 Bodansky units. A cephalin-flocculation test was +++ in twenty-four hours and ++++ in forty-eight hours. The bleeding time was one and a half and the clotting time five minutes. On the twentieth hospital day the patient developed edema of the scrotum and prepuce. The radiosodium space was found to be 34 per cent of the body weight, and the thiocyanate space 43 per cent.*

On the twenty-second hospital day the patient began to vomit blood and passed grossly bloody stools. Gastrointestinal bleeding lasted for four days, and numerous blood transfusions were required to keep the patient out of shock. Four days later another 5700 cc of abdominal fluid was removed, following which the patient appeared some-

what improved. A van den Bergh test was 3.2 mg direct and 5.8 mg total. On the thirty-third hospital day an x-ray film of the chest revealed a posterolateral fracture of the eighth rib that had not been seen previously. There were still areas of increased density in both lower lung fields. The ascites appeared to be forming more rapidly with each tap, and ankle edema was becoming noticeable. On the forty-first hospital day the blood phosphorus was 2.6 mg per 100 cc, the alkaline phosphatase 100 Bodansky units and the total protein 6.77 gm per 100 cc, with an albumin-globulin ratio of 0.5. The bromsulfalein test (2 mg per kilogram of body weight) showed 95 per cent retention of the dye after thirty minutes. On the forty-third hospital day the patient again began to vomit blood, and on the following morning the temperature suddenly spiked to 105°F. The patient continued to vomit blood and to pass tarry stools. He went into shock and coma, but the systolic blood pressure returned to 150 after a transfusion. Nevertheless, the patient remained unresponsive, with the eyes half open and wandering from side to side and with the pupils rather large and responding to light. The legs and arms were extended and rigid, but the neck was not stiff. Arm and leg reflexes were hyperactive, and there was a positive Babinski sign on the right. The patient's condition remained unchanged, except that the arms gradually became flaccid. On the morning of the forty-fifth hospital day respirations became gasping and ceased.

DIFFERENTIAL DIAGNOSIS

DR J WALLACE ZELLER. The history is that of a patient with long-standing liver disease who developed rather rapidly progressive hepatic failure and portal obstruction. His death was preceded by bleeding from esophageal varices and possibly also by a terminal event involving the central nervous system.

The summary suggests that the patient had the hepatic facies. Ascites was obvious. A liver two or three fingerbreadths below the costal margin is probably enlarged if the upper level of dullness is in the fifth intercostal space. Apparently the liver was not noted to be definitely nodular. The spleen was not commented on, so that it may be assumed that it was not felt.

The low white-cell count and the alterations in the serum protein are frequently found in severe liver disease. No comment concerning jaundice is made, although the van den Bergh reaction rose to a total of 5.8 mg. At that level clinical jaundice is usually evident. The epistaxes and hematomas of the lower legs are probably related to the prolonged prothrombin time and the alteration in vitamin K metabolism associated with severe liver disease. The results of the bromsulfalein tests reveal marked hepatic insufficiency. The elevation in serum cholesterol, the low serum vitamin A level,

*These measurements were carried out in the surgical research laboratories where normal values for extracellular fluid volume average around 20 per cent of the body weight. Values over 33 per cent of the body weight are usually correlated with gross disturbances of electrolyte metabolism in which ions normally extracellular in position appear to move within the intracellular space. Values between 20 and 33 per cent of the body weight are associated with various grades of clinical edema. (Moore F. D. Determination of total body water and solids with isotopes. *Science* 104: 157-160, 1946.)

elevated alkaline phosphatase and the abnormal phalin-flocculation tests are all changes that might be expected in diffuse liver disease.

The record gives no history of definite injury, which may have been a cause for the fracture of the eighth rib. The fracture was present on the right side and may well have caused the pain in the right anterior chest that was brought on by coughing and raising the right arm. This lesion of course may have been a cough fracture, since we are informed that a persistent hacking cough was present for six weeks before entry. This was most probably due to bronchitis. The areas of atelectasis and collapse that developed may have been due to collections of mucus in the bronchi and small bronchial radicles.

The combination of hepatic failure and portal obstruction naturally brings cirrhosis of the liver to the fore as the likeliest diagnostic possibility. In explaining the etiology of such a lesion we are given at least three possibilities by the history. These are in the order of likelihood: alcohol, syphilis and arsenical antisyphilitic therapy. I believe that we may assume that the intravenous injections the patient was receiving when he became jaundiced were arsphenamine or nearsphenamine. The fact that the jaundice disappeared while the injections were continued makes it unlikely that he had a true arsenical hepatitis. It should be stated that the continuance of arsenical therapy in the presence of jaundice is fearless but unjustified treatment for syphilis. There is a good possibility of producing acute yellow atrophy by such means. The cirrhosis that develops following injury to the liver from arsenic is not true portal cirrhosis. Syphilis itself can cause cirrhosis of the portal type. This patient's syphilitic infection was irregularly, and therefore inadequately, treated. The history and findings are consistent in every way with a diagnosis of alcoholic cirrhosis of the liver. The possibility that alcohol and one or more of the other two factors were simultaneously involved must be considered.

An additional etiologic factor that sometimes causes jaundice in patients receiving arsenical antisyphilitic treatment is epidemic infectious hepatitis. Cases in which this has been traced in clinics to improperly cleaned needles and syringes have been reported. In this regard it is of interest to note that studies of liver biopsies of patients with epidemic infectious hepatitis, arsenical hepatitis and homologous serum jaundice reveal no definite histologic differences in the three conditions.

The gastrointestinal bleeding, which was a prominent feature of the terminal course, undoubtedly had its origin in the esophageal varices. The increased van den Bergh reaction noted at that time may have been partially due to the absorption of blood pigment from the intestine.

During the last day of life the patient was in coma. Various transient paralyses may occur in so-called "hepatic coma." The changes described could have

been due to a left-sided cerebral hemorrhage, possibly associated with the rupture of a syphilitic aneurysm. The extension and rigidity of the extremities could be interpreted as a manifestation of cerebral irritation preceding the stage of paralysis and flaccidity. It is entirely possible that these terminal manifestations could occur without bleeding into the brain, however.

There is good evidence from the history and serologic reactions that this patient had syphilis. Aside from a possible syphilitic factor as a contributing cause of the liver disease and the less likely presence of a syphilitic cerebral aneurysm, there is little evidence from this record of syphilis of other organs. That does not mean, of course, that it will not be found.

My final diagnosis is portal cirrhosis of the liver, with bleeding esophageal varices, ascites and final hepatic failure. It is entirely possible that some fresh destructive lesions of the liver cells will be found, in addition to the old cirrhosis. Alcohol and possibly syphilis are the likeliest etiologic factors to be associated with the cirrhosis. Arsphenamine or infectious hepatitis may have played a contributing role, although they are not usually considered causes of typical portal cirrhosis.

CLINICAL DIAGNOSES

Cirrhosis of liver, ? type
Cerebral hemorrhage or thrombosis

DR ZELLER'S DIAGNOSES

Portal cirrhosis of liver
Bleeding esophageal varices
Ascites
Hepatic failure

ANATOMICAL DIAGNOSES

Hepatoma, with portal vein invasion and thrombosis
Cirrhosis of liver, alcoholic type
Esophageal varices, with massive hemorrhage
Ascites
Necrotizing bronchopneumonia
Fibrous pleuritis
Arteriosclerosis, generalized and coronary
Healing fractures, right seventh and eighth ribs

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY: This patient showed, as Dr Zeller predicted, a severe cirrhosis of the liver, with esophageal varices from which the numerous attacks of bleeding had come. There was, however, something more. The liver was significantly enlarged, weighing over 2200 gm, and the surface showed a combination of coarse nodularity and fine granulation. On section it was obvious that a large part of the liver had been replaced by tumor, which was spreading in the form of thrombi throughout the intrahepatic portal vein. The thrombus ex-

tended back about 1 cm in the portal vein beyond its point of exit from the liver substance. The identifiable hepatic veins were free from tumor. It is somewhat more usual to find invasion of the hepatic rather than the portal vein. The process was so extensive in this case that the portal obstruction must have been complete. On microscopic examination the tumor proved to be a characteristic hepatoma, with an excellent grade of differentiation, leaving no room for doubt regarding the diagnosis. In the portion of the liver not invaded by tumor a finely granular cirrhosis was present. There were many foci of fresh infarct-like necrosis, presumably due to the venous obstruction. Too little of the cirrhotic portion was uninvolved to permit a definite opinion concerning the type of cirrhosis, it was quite compatible with an alcoholic type. Dr. Zeller avoided the trap of assuming that the rib fracture, without a clear history of trauma, was a pathologic fracture due to metastases. Section through the area of fracture showed active bone callus but no evidence of tumor.

Despite the profound central-nervous-system symptoms the brain showed relatively little. There were no gross areas of hemorrhage or softening, and the arterial system showed no point of occlusion. There was a slight granularity of the ependyma, and a few perivascular foci of lymphocytes could be found. These are compatible with a low grade of central-nervous-system syphilis, and it is doubtful if they were connected in any way with the hepatic insufficiency. Experience with the fulminating type of hepatitis during the war made many of us familiar with the marked central-nervous-system symptoms that may accompany hepatic insufficiency. I saw a few patients with hepatitis who died so rapidly that jaundice never developed. In these patients the central-nervous-system symptoms completely dominated the clinical picture. The anatomic findings in the brain were always disappointing. Slight clouding of the meninges and occasional foci of perivascular cuffing were all that was ever seen. The situation is analogous to that in uremia, in which, again, prominent central-nervous-system symptoms are present but minimal nonspecific lesions can be found only in the brain.

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WORLD HUNGER

DESPITE the inevitable association between war and famine, when the ploughshare is beaten into a sword and the farmer must leave his field to wield the sword, the present world famine goes deeper even than the recent world war. Ploughed fields, it is true, have been trampled into mud by the hurrying feet of the world's greatest armies and torn asunder by the destructiveness of their machines, but Nature has also set the stage for her own act in this common disaster.

Over two years ago, in the summer of the Southern Hemisphere, according to a recent issue of *Future*, Latin America was visited with its worst drought in eighty-six years. Argentina's wheat production fell to 60 per cent of normal, and her corn crop to a

third, while Cuba's sugar crop practically dried up at the source. At the same time a drought affected North Africa, breadbasket of France and the Mediterranean basin, so that by the end of 1945 the grain output of this region had dropped from four million to scarcely one million tons. Half the wheat crop and most of the potatoes and beans were failing in South Africa, and this section had to import food by the end of 1945, Australia went dry, and the worst drought in modern times, following heavy rains, destroyed the 1945 crops of the Danube basin. This drought also visited Italy, Spain, France and the Low Countries. Finally the rains have failed in India, Ceylon and Burma, the last-named country being the world's largest exporter of rice. In addition, rinderpest has struck Burma's work cattle, killing a large proportion of them. This year Burma will have no rice to export.

Apparently only the United States, Canada, part of the Middle East and perhaps imponderable Russia are continuing to raise bumper crops, and they must tide over the rest of the world until it can again begin to feed itself. Mass starvation, it is said, has been averted for the time being, but mass malnutrition is dangerously close to the line, and this will prevail at least until the 1947 crops are harvested.

The Department of Agriculture announced in June the failure of this country to meet its export goal of grain and fats and oils for the first quarter of the year, the report of the Secretary of Agriculture to the President on July 8 announced that the fiscal year's grain commitment of 400 million bushels had been met by June 30. This shipment, moreover, was nearly double the requirement for the year that was presented to the Combined Food Board a year ago. Figures, particularly astronomical figures, have little meaning for the individual, impressive as they may appear. Thus, it means little to learn that we have exported, during the fiscal year, 16,700,000 long tons of food unless we know what relation this bears to our normal exports, to our total production, to the exports of other food-producing countries and, particularly, to the world's present needs.

We are passing through an unprecedented period of famine. Are we doing our share in its control, and how successful can we expect its control to be?

COMBINED SULFONAMIDE AND PENICILLIN THERAPY

THE desirability of using both sulfonamides and penicillin in the treatment of infections that are susceptible to both agents is a practical everyday problem. It is amenable, in part, to study in the test tube and in experimental infections of animals, but the final answer must come from a careful analysis of many factors and particularly from the results of clinical experience.

Most but not all of the experimental evidence suggests that the combined use of both agents is preferable to the use of either one alone. Ungar¹ reported that sulfapyridine has a synergistic effect on the action of penicillin against *Staphylococcus aureus* and *Streptococcus haemolyticus* in vitro and in mice. Bigger^{2, 3} found that sulfathiazole increases the dilution in which the inhibitory action of penicillin takes place. He therefore advocated the combined use of the two agents in staphylococcal infections and suggested that the combination might even prove effective against the typhoid bacillus. Kirby⁴ also demonstrated that urea-penicillin and sulfonamide-penicillin mixtures produce greater bacteriostasis of cultures of staphylococci than does penicillin alone. This, however, he found to be purely an additive effect and not a potentiation, since the combination was not inhibitory in concentrations that did not inhibit separately.

The differences in the mode of action of the sulfonamides and of penicillin should be borne in mind. Hobby and Dawson⁵ found that penicillin is most effective during the active multiplication of bacteria and that the concentration of the organisms, within fairly wide limits, is not important so long as multiplication occurs and a sufficient concentration of penicillin is present. The sulfonamides, on the other hand, they⁶ found to be effective only after a lag period during which the organisms multiply while in contact with the drug. Sulfonamides added after organisms had passed the growth acceleration phase produced no bacteriostasis. In addition, the sulfonamides did not act on large numbers of organisms even if they were actively multiplying. They concluded that there was no evidence of any synergistic action of sulfonamides on penicillin.

They also thought that para-aminobenzoic acid⁷ did not increase the effective titer of penicillin but did increase its rate of action, presumably under conditions in which it enhances growth.

More detailed studies by Hobby and Dawson⁵ showed that the results obtained with the combined use of penicillin and sulfadiazine are dependent on many factors. Among these are the concentration of each bacteriostatic agent, the number of organisms present, the environmental conditions allowing growth of the organisms, the susceptibility of the organism to the two agents and the organisms involved.

When penicillin was present in amounts so small as to produce little or no bacteriostasis, sulfadiazine increased the bacteriostatic action provided that the organism was sensitive to the sulfonamide and was present in small numbers. In the presence of an amount of penicillin that by itself was sufficient to produce a definite bacteriostatic or bactericidal effect during the first few hours of incubation but insufficient to yield complete sterilization, sulfadiazine increased bacteriostasis, but again, this occurred only when the number of organisms at the end of the sulfadiazine lag was low. Hobby and Dawson thought that the sensitivity of the organism to sulfadiazine enhanced this effect, but that the degree of sensitivity did not necessarily have to be sufficient to be demonstrable by the usual methods.

With larger amounts of penicillin, its bactericidal action was rapid during the first few hours of incubation and complete sterilization often resulted within five to seven hours. If sterilization was not complete at the end of that time, the presence of sulfadiazine sometimes actually prolonged the lag period or even slightly decreased the bactericidal rate. It appears, therefore, that since the action of penicillin occurs predominantly at the time of cell division, a decrease in the rate of multiplication due to sulfadiazine can decrease the rate at which penicillin acts.

The results of similar studies were briefly reported by Vigouroux and Leyton.⁸ They found that the antibiotic action of penicillin for a number of strains of pathogenic bacteria was reinforced over a wide range by the addition of small amounts of either sulfathiazole, sulfapyridine, sulfadiazine or para-

benzoic acid The incorporation of one of the sulfonamides and para-aminobenzoic acid in the solution with penicillin nullified the potentiation. A penicillin-para-aminobenzoic acid mixture had a more pronounced action on penicillin-sensitive strains, however, than did a combination of penicillin and one of the sulfonamides. The sensitivity of the organism to penicillin played no part in the latter potentiation but, according to these authors, was related to the intrinsic antibacterial action of the substance under investigation. Occasional organisms were encountered that were susceptible to penicillin-sulfonamide mixtures but resistant to each agent applied separately. On the basis of their results, these authors thought that the combination of sulfonamides and penicillin is indicated in certain infections.

There are clinical conditions in which sulfonamides have been found empirically to add to the effect of penicillin. This is particularly true in cases of meningitis due to organisms that are susceptible to both. In such cases the mortality obtained with the combined use of sulfonamides and penicillin, the latter given both intrathecally and intramuscularly, is lower than that obtained with either antibacterial agent used alone. Probably similar results may be expected in other bacterial infections in which there is a tendency of the infection to focalize in inaccessible areas. In such conditions the problems of penetration and diffusion into the infected foci may be an important factor. Differences in the susceptibility of the organisms and the possible additive effect of the two agents, however, may also be significant.

Evidence suggesting that penicillin diffuses into fibrin clots whereas sulfonamides do not⁹ may help to explain the better results obtained with the former in cases of bacterial endocarditis and possibly also in some cases of empyema. The failure of penicillin to penetrate in adequate amounts into the cerebrospinal fluid after systemic administration and probably also the greater susceptibility of the bacterial strains to sulfonamides may account for the better results obtained with sulfadiazine in cases of meningococcal meningitis. Combined therapy has not usually proved advantageous in these circumstances.

In the last analysis, the question of the clinical use of combined penicillin and sulfonamides must be considered as a problem to be decided according to the particular circumstances of any given case. Among other factors one must take into account the desirability of giving frequent injections of penicillin or of subjecting the patient to the possible toxic effects of the sulfonamides. A large increase in the dosage of penicillin is usually more effective than the additional use of sulfonamides. Combined therapy is usually reserved for the severest cases and seems to produce the best results in such cases. This has recently been shown to be true in pneumonia¹⁰ as well as in meningitis.

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MORRISON, BENJAMIN G, Veterans Administration Hospital,
Northampton
Long Island College of Medicine, 1931

STEINBERG, IRVING H, Cooley Dickinson Hospital,
Northampton
Medical College of the State of South Carolina, 1941

STRAUSS, ELLIOT G, Cooley Dickinson Hospital, Northamp-
ton.
Tufts College Medical School, 1943

WAITE, HAROLD M, 1 Clark Street, Easthampton
Middlesex University School of Medicine, 1937 Sponsor
L Beverly Pond, 115 Main Street, Easthampton

Mary Poland Snook, *Secretary*
Worthington

MIDDLESEX EAST DISTRICT

BRIGGS, BERNARD D, 14 South Street, Stoneham
College of Medical Evangelists, 1940

GRANT, W MORTON, 7 Pierrepont Road, Winchester
Harvard Medical School, 1940

KILLAM, ARTHUR R, 1 Parker Road, Winchester
Boston University School of Medicine, 1944

McLAUGHLIN, LAURENCE S, 80 Main Street, Woburn
Tufts College Medical School, 1943

SPRAGUE, MARION L, New England Sanitarium and Hospital,
Stoneham
College of Medical Evangelists, 1943

WEBSTER, RICHARD C, JR., Chandler Road, Burlington
Harvard Medical School, 1943

Roy W Layton, *Secretary*
8 Porter Street, Melrose

MIDDLESEX NORTH DISTRICT

BAILEY, DAVID B, 561 Rogers Street, Lowell
Tufts College Medical School, 1940

KAHN, WALTER, 68 Littleton Road, Chelmsford
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East Merrimack Street, Lowell

KALDECK, ROBERT, 75 Robbins Street, Lowell
University of Vienna, 1935 Sponsor John J McNamara,
63 Kirk Street, Lowell

KENNEDY, ARTHUR P, 77 Mansur Street, Lowell
Tufts College Medical School, 1942

Brendan D Leahey, *Secretary*,
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Boston University School of Medicine, 1938

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Boston University School of Medicine, 1942

BERK, MORTON S, 59 Philbrick Road, Newton Centre
Boston University School of Medicine, 1940

BOYLE, JEREMIAH J, JR., 1737 Cambridge Street, Cambridge.
Tufts College Medical School, 1943

BRIDGES, WILLIAM C, 1016 Beacon Street, Newton Centre.
Yale University School of Medicine, 1940

BRUNO, SALVATORE J, 11 Yale Street, Medford
New York Medical College, 1943

CARADONNA, MATTEO, 132 Chelsea Street, Everett
Middlesex University School of Medicine, 1938 Sponsor
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CARP, JACOB S, 206 Elliot Street, Newton Upper Falls
Middlesex University School of Medicine, 1940 Sponsor
Israel Kahalas, Newton, office, 483 Beacon Street, Boston

DENNEHY, TIMOTHY J, 106 Algonquin Road, Chestnut Hill
Georgetown University School of Medicine, 1944

ETTENBERG, MAX, 120 White Street, Belmont
Middlesex University School of Medicine, 1940 Sponsor
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FEINGOLD, MYER, 584 Salem Street, Malden
Middlesex University School of Medicine, 1937 Sponsor
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GLICKLICH, EARL A, 81 Undine Road, Brighton
University of Cincinnati College of Medicine, 1938

GOLDBERG, M Milton, Malden Hospital, Malden
Tufts College Medical School, 1940

GORFINE, MORRIS, 144 Jaques Street, Somerville
Middlesex University School of Medicine, 1938 Sponsor
Robert Gorfine, 120 Brainerd Road, Allston

GRODEN, HAROLD M, 1531 Cambridge Street, Cambridge
Tufts College Medical School, 1939

HIRSCH, LAWRENCE S, 42 Lincoln Street, Framingham
Middlesex University School of Medicine, 1940 Sponsor
Frederick H Salls, 132 Union Avenue, Framingham

HOFFMAN, JOHN L, 7 Arlington Street, Cambridge
University of Buffalo School of Medicine, 1924

LEVENSON, HERBERT M, 141 Sutherland Road, Brighton
Boston University School of Medicine, 1940

LEVINSON, LEON, 40 Cloverdale Road, Newton Highlands
Tufts College Medical School, 1943

LEVREAULT, GERALD V, 26 Chase Street, Newton Centre
Tufts College Medical School, 1942

McARTHUR, JANET W, 204 Pleasant Street, Arlington
Northwestern University Medical School, 1942

MONAGHAN, LEO B, Old Road to Nine Acre Corner, Concord
Tufts College Medical School, 1943.

MOSEH, HENRY A, 11 Beatrice Circle, Belmont
Northwestern University Medical School, 1938

O'HARA, JOHN L, 136 Hunnewell Avenue, Newton
Tufts College Medical School, 1941

OSBORNE, MELVIN P, 20 Rogers Street, Newton Highlands
Harvard Medical School, 1942

PAUL, DAVID M, 91 Irving Street, Everett.
Middlesex University School of Medicine, 1937 Sponsor
Burton C Grodberg, 640 Main Street, Malden

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Middlesex University School of Medicine, 1940 Sponsor
David D Sher, 133 West Main Street, Marlborough
- SCARINGI, JOSEPH, 66 Curtis Street, West Somerville
Middlesex University School of Medicine, 1937 Sponsor
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Harvard Medical School, 1915
- SOMMERS, SHELDON C, 57 Kenwood Avenue, Newton Centre
Harvard Medical School, 1941
- STEIMAN, SOLOMON E, 1874 Commonwealth Avenue,
Brighton
Boston University School of Medicine, 1943
- SWANK, ROY L, 105 Wood End Road, Newton Highlands
Northwestern University Medical School, 1935
- TIERNEY, THOMAS M, 1980 Commonwealth Avenue,
Brighton
Georgetown University School of Medicine, 1942
- TRODELLA, GEORGE P, 95 Pearl Street, Somerville
Tufts College Medical School, 1943
- TULLIS, JAMES L, 9 Billings Park, Newton
Duke University School of Medicine, 1940
- WARREN, KENNETH W, 1371 Walnut Street, Newton High-
lands
Temple University School of Medicine, 1938
- WILHELM, NORBERT A, 160 Lake Avenue, Newton Centre
St Louis University School of Medicine, 1925
- WILLIAMS, NATHAN, 264 Kelton Street, Allston
Boston University School of Medicine, 1939
- WOODS, FRANCIS M, 60 Brush Hill Road, Newton Highlands
Yale University School of Medicine, 1933
- WORCESTER, JOHN, 87 Allen Avenue, Waban
Tufts College Medical School, 1939
- WYMAN, STANLEY M, 840 Massachusetts Avenue, Arlington
Harvard Medical School, 1939
- YORK, RICHARD F, 918 Chestnut Street, Waban
Middlesex University School of Medicine, 1940 Sponsor
Laurence J Louis, 1515 Centre Street, Newton Centre
- Alexander A Levi, Secretary
481 Beacon Street, Boston

NORFOLK DISTRICT

- ALEXANDER, EBEN, JR, 27 Longwood Avenue, Brookline
Harvard Medical School, 1939
- ALFORD, HYMAN, 4 Thane Street, Dorchester
Tufts College Medical School, 1941
- BARTOL, GEORGE M, 126 Woodlawn Avenue, Wellesley Hills
University of Pennsylvania School of Medicine, 1939
- BLUESTEIN, LOUIS L, 60 Lincoln Street, Hyde Park
Middlesex University School of Medicine, 1941 Sponsor
Charles Korb, 1259 Hyde Park Avenue, Hyde Park
- BRADON, JOSEPH H, 93 Common Street, Dedham
Columbia University College of Physicians and Surgeons,
1939.
- BROOKS, EUGENE F, Wrentham
Middlesex University School of Medicine, 1939 Sponsor
Karl V Quinn, Wrentham State School, Wrentham
- BROWN, FRANCIS H, 31 Monadnock Road, Wellesley Hills
Tufts College Medical School, 1941
- CARROLL, JOHN J, 107 Harvard Street, Dedham
Tufts College Medical School, 1931
- CHAPMAN, CARLETON B, 295 Walnut Street, Brookline
Harvard Medical School, 1941
- CLINTON, MARSHALL, JR, 324 Linden Street, Wellesley
University of Buffalo School of Medicine, 1940
- COBURN, MORTON B, 48 Browne Street, Brookline
Middlesex University School of Medicine, 1939 Sponsor
Benjamin F Sieve, 134 Sewall Avenue, Brookline
- COHEN, SIDNEY, 214 Riverway, Boston
Harvard Medical School, 1937
- COLEMAN, NATHAN W, 38 Greendale Road, Mattapan
Middlesex University School of Medicine, 1941 Sponsor
Eli Friedman, Roxbury, office, 416 Marlboro Street, Boston
- COX, GEORGE E, 38 Highland Street, Hyde Park
Middlesex University School of Medicine, 1935 Sponsor
Irving J Shalett, 1589 Beacon Street, Brookline
- CURLEY, GEORGE A, 853 Cummins Highway, Mattapan.
College of Physicians and Surgeons, Boston, 1937
Sponsor Henry L Pelkus, 15 Fairmount Avenue, Hyde
Park
- ECHLOV, THEODORE G, 112 Salisbury Road, Brookline
Middlesex University School of Medicine, 1940 Sponsor
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Boston
- EHRENBERG, RUTH, Boston State Hospital, Dorchester
University of Berlin, 1926 Sponsor Walter E. Barton,
Boston State Hospital, Dorchester
- EMERSON, KENDALL, JR, 71 Griggs Road, Brookline
Harvard Medical School, 1933
- ENGLAND, ALBERT C, JR, 42 Griggs Terrace, Brookline
Harvard Medical School, 1937
- FOX, HENRY M, 17 Clark Road, Wellesley Hills
Johns Hopkins University School of Medicine, 1933
- FRECHETTE, ALFRED L, 673 High Street, Westwood
University of Vermont College of Medicine, 1934
- GOLDBERG, IRVING E, 103 Winthrop Street, Roxbury
Medical College of the State of South Carolina, 1940
- HASTINGS, NELSON, 70 Cypress Street, Brookline
Harvard Medical School, 1940
- HAYDEN, CHARLES G, 59 Vernon Street, Brookline
University of Minnesota Medical School, 1941
- HERMANSON, ROBERT H, 268 Mason Terrace, Brookline
Tufts College Medical School, 1939
- KALDECK, RUDOLPH, 591 Morton Street, Dorchester
University of Vienna, 1912 Sponsor Walter E Barton
Boston State Hospital, Dorchester
- KARRAS, JOSEPH D, 82 Stedman Street, Brookline
Middlesex University School of Medicine, 1937 Sponsor
George A Small, 81 Walpole Street, Norwood
- KELLEY, THOMAS F, 384 Boylston Street, Brookline
Boston University School of Medicine, 1939
- KICKHAM, EDWARD T, 657 Chestnut Hill Avenue, Brookline
Tufts College Medical School, 1941
- LARCOM, RODNEY C, JR, 481 Washington Street, Dedham
Harvard Medical School, 1940
- LAYTON, MANUEL L, 50 Winston Road, Dorchester
Middlesex University School of Medicine, 1932 Sponsor
Jacob Applebaum, 371 Commonwealth Avenue, Boston
- LENSON, NORMAN, 55 Wilcox Street, Dorchester
Tufts College Medical School, 1943
- LEVINE, ALBERT, 939 Morton Street, Mattapan
Middlesex University School of Medicine, 1937 Sponsor
Samuel L Marnoy, Brookline, office, 311 Commonwealth
Avenue, Boston
- LEWENSTEIN, HOWARD J, 9 Leland Road, Brookline
Tufts College Medical School, 1942
- LEWIS, ROGER A, 38 Kilsyth Road, Brookline
Johns Hopkins University School of Medicine, 1938
- LOTH, ERIC C, 28 Montebello Road, Jamaica Plain
Middlesex University School of Medicine, 1939 Sponsor
Arnold N Allen, 961 South Street, Roslindale
- LYNCH, ALICE D, 28 Bellevue Street, Dorchester
Tufts College Medical School, 1930
- MALOOF, EMIL G, 3 New Park Avenue, West Roxbury
Middlesex University School of Medicine, 1936 Sponsor
Antonio P Milone, 4354 Washington Street, Roslindale
- McCOMBS, ROBERT P, 1514 Beacon Street, Brookline
University of Pennsylvania School of Medicine, 1935
- McNAMARA, THOMAS J, 58 St Rose Street, Jamaica Plain
Tufts College Medical School, 1942
- MELINE, DAVID I, 72 Maywood Street, Roxbury
Middlesex University School of Medicine, 1937 Sponsor
Benjamin F Bornstein, Chestnut Hill, office, 370 Commos
wealth Avenue, Boston
- MORRISON, HERBERT S, 89 Englewood Avenue, Brookline
McGill University Faculty of Medicine, 1945
- MORSE, LAWRENCE S, 73 Thatcher Street, Brookline.
Tufts College Medical School, 1938

- D'BRIEY, JOSEPH A, 11 Shenandoah Street, Dorchester
Tufts College Medical School, 1941
- D'BRIEN, PAUL I, 102 Wheatland Avenue, Dorchester
Tufts College Medical School, 1942
- D'CONNELL, WILLIAM T, 40 Murray Hill Road, Roslindale
Tufts College Medical School, 1943
- PARK, IRVING H, 64A University Road, Brookline
Middlesex University School of Medicine, 1937 Sponsor
Thomas P Kendrick, 454 Washington Street, Brookline
- PIER, ARTHUR S., JR., 539 Brush Hill Road, Milton
Harvard Medical School, 1939
- PILEA, DOMINIC, 40 Mill Street, Dorchester
Middlesex University School of Medicine, 1929 Sponsor
Paul J Jakmauh, Milton, office, 509 Broadway, South Boston
- POWERS, HAZEL C KANZ, 74 Fenwood Road, Boston
Middlesex University School of Medicine, 1924 Sponsor
Elizabeth Z Kleinman, 66 Perkins Street, Jamaica Plain.
- POWERS, JOSEPH W, 121 Blue Hill Avenue, Roxbury
Kansas City University of Physicians and Surgeons, 1937
Sponsor Bernard A Godvin, Jamaica Plain, office, 483
Beacon Street, Boston
- POTNAM, HENRY M, 151 Grove Street, Westwood
Harvard Medical School, 1935
- RAND, HARRY, 16 Baird Street, Dorchester
Middlesex University School of Medicine, 1935 Sponsor
Charles Silverstein, 99 Stratton Street, Dorchester
- ROODIN, HARRY, 100 Seaver Street, Roxbury
College of Physicians and Surgeons, Boston, 1940 Sponsor
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Boston
- ROSEN, DANIEL, 66 Columbia Road, Roxbury
University of Vienna, 1936 Sponsor Hyman B Goldberg,
2 Pasadena Road, Dorchester
- ROSMARTIN, ERNEST, 14 Autumn Street, Boston
University of Vienna 1906 Sponsor Hyman Morrison,
Brookline, office, 483 Beacon Street, Boston
- SHAPIRO, ELI, 484 Blue Hill Avenue, Roxbury
Middlesex University School of Medicine, 1937 Sponsor
George Rohhins, Brookline, office, 416 Marlboro Street,
Boston
- SWARTZ, MORRIS, 22 Wentworth Terrace, Dorchester
Boston University School of Medicine, 1935
- TRIBBY, WILLIAM W, 198 Aspinwall Avenue, Brookline
Harvard Medical School, 1937
- WELCH, C STUART, 170 Dudley Street, Brookline
Tufts College Medical School, 1932
- WISE, H ROBERT, 36 Schuyler Street, Roxbury
Middlesex University School of Medicine, 1936 Sponsor
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- ZINDWER, RENEE, 4076 Washington Street, Roslindale
University of Vienna, 1938 Sponsor Marjorie Woodman,
Jamaica Plain, office, 21 Bay State Road, Boston

Basil E Barton, *Secretary*
10 Richwood Street, West Roxbury

NORFOLK SOUTH DISTRICT

- AMERENA, JOHN P, 230 North Main Street, Randolph
Middlesex University School of Medicine, 1937 Sponsor
Edmund B FitzGerald, 563 Furnace Brook Parkway,
Quincy
- BALLIN, LUDWIG, Norfolk County Hospital, South Braintree
University of Munich 1924 Sponsor Nahum R Pills-
bury, Norfolk County Hospital, South Braintree
- COLLINS, GERALD M, 4 High Street, Hingham
Boston University School of Medicine, 1941
- HECHT, PAUL L, 426 Washington Street, Braintree
University of Freiburg 1920 Sponsor Clifford F Dan-
forth 165 Washington Street, Weymouth
- MILLEN, MORRIS H, 391 Bridge Street, North Weymouth
Middlesex University School of Medicine, 1933 Sponsor
William S Altman 32 Spear Street, Quincy

- NEVINS, SIMON H, 611 Adams Street, Quincy
Middlesex University School of Medicine, 1925 Sponsor
Harry Braverman, 43 School Street, Quincy
- SLOANE, WILLIAM C, 15 South Main Street, Randolph
Middlesex University School of Medicine, 1933 Sponsor
Frank W Crawford, 98 North Franklin Street, Hollbrook

Ebenezer K Jenkins, *Secretary*
Norfolk County Hospital, South Braintree

PLYMOUTH DISTRICT

- ARNONE, WILLIAM H, 147 Myrtle Street, Brockton
New York University College of Medicine, 1942
- CARPINELLA, CHARLES J, 94 Moraine Street, Brockton
Middlesex University School of Medicine, 1931 Sponsor
Victor V Ragonetti, 145 Court Street, Plymouth
- DESIMONE, JOHN S, 145 West Elm Street, Brockton
Middlesex University School of Medicine, 1939 Sponsor
John A Carriuolo, 290 Forest Avenue, Brockton
- DONNELLY, JAMES F, 63 Franklin Avenue, Rockland
Middlesex University School of Medicine, 1939 Sponsor
Joseph H Dunn, 321 Union Street, Rockland
- ENOS, ALLEN W, Broadway, Hanover
Middlesex University School of Medicine, 1939 Sponsor
Joseph H Dunn, 321 Union Street, Rockland
- MAYO, WALTER V, 119 Summer Street, Kingston
Middlesex University School of Medicine, 1936 Sponsor
George A Moore, 167 Newbury Street, Brockton
- MCCLOSKEY, JOHN E, 932 Main Street, Brockton
Middlesex University School of Medicine, 1940 Sponsor
Joseph S Phaneuf, 688 North Main Street, Brockton
- MOORE, KENNETH T, Washington Street, Hanover
Hahnemann Medical College, 1936
- POTNAM, ROBERT M, 31 North Street, Plymouth
McGill University Faculty of Medicine, 1944
- SHEEHAN, JOHN C, Marginal Street, Green Harbor
Tufts College Medical School, 1943
- WEISS, SAMUEL, 47 West Elm Street, Brockton
Tufts College Medical School, 1930

Ralph C McLeod, *Secretary*
Goddard Hospital, Brockton

SUFFOLK DISTRICT

- ALBERT HAROLD S, 476 Beacon Street, Boston
McGill University Faculty of Medicine, 1943
- CANNON, RAYMOND G, 158 O Street, South Boston
Middlesex University School of Medicine, 1940 Sponsor
John J Todd, 587 Beacon Street, Boston
- CAPODILUPPO, GRAZIANO A, 109 Prince Street, Boston
Middlesex University School of Medicine, 1935 Sponsor
Anthony O Cardullo, 261 Hanover Street, Boston
- CARTER, BARBARA F, 256 Beacon Street, Boston
Tufts College Medical School, 1942
- FORD, RICHARD, 157 Newbury Street, Boston
Harvard Medical School, 1940
- GOLDEN, ISAAC, 174 Chestnut Street, Chelsea
Middlesex University School of Medicine, 1936 Sponsor
Benjamin I Cassin, 195 Chestnut Street, Chelsea
- GUARCIARELLO, COSMO A, 131 Endicott Street, Boston
Royal University of Rome, 1935 Sponsor E Parker
Hayden, 270 Commonwealth Avenue, Boston
- HARRIS, OLIVER J, 334 Beacon Street, Boston
Tufts College Medical School, 1940
- HELMAN, MILTON E, 18 Lynn Street, Chelsea
Boston University School of Medicine, 1940
- HINTON, ELMER E, 386 Commonwealth Avenue, Boston
University of Kansas School of Medicine, 1941
- KENNAN, FRED J, 1 James Street, Boston
Tufts College Medical School, 1935
- KING, MYRON N, 132 Shore Drive, Winthrop
University of Vermont College of Medicine, 1941
- LUONGO, ANGELO J, 17 Vinal Street, Revere
Middlesex University School of Medicine, 1934 Sponsor
Harold L Musgrave, 620 Beach Street, Revere

- McKEIGUE, JOHN E., 3 Poplar Place, Boston
Jefferson Medical College of Philadelphia, 1942
- MILLER, HAROLD, 48 Addison Street, Chelsea
Midwest Medical College, 1937 Sponsor Aubrey C Benjamin, 35 Eleanor Street, Chelsea
- MYERSON, PAUL G., 66 Fenway, Boston
Harvard Medical School, 1939
- PAULL, THOMAS, Boston City Hospital, Boston
Harvard Medical School, 1940
- PIPI, JOHN, 821 Saratoga Street, East Boston
Middlesex University School of Medicine, 1935 Sponsor Pasquale Costanza, 238 Maverick Street, East Boston
- PRESCOTT, BLAKE D., 41 Deerfield Road, Wethersfield, Conn
Middlesex University School of Medicine, 1931 Sponsor Davis T. Gallison, 520 Commonwealth Avenue, Boston
- RECORD, EUGENE E., 308 Commonwealth Avenue, Boston
McGill University Faculty of Medicine, 1937
- RIPA, ANTHONY S., 523 Beacon Street, Boston
Middlesex University School of Medicine, 1936 Sponsor Louis Cohen, 108 Meridian Street, East Boston
- RUFF, JOHN J., 39 North Russell Street, Boston
Washington University School of Medicine, 1944
- VITERBI, ACHILLE, 250 Commonwealth Avenue, Boston
University of Turin, 1905 Sponsor Carl F. Maraldi, 276 Commonwealth Avenue, Boston
- WEINBERGER, JEROME L., 117 Bay State Road, Boston
New York University College of Medicine, 1938
- WOLFE, LOUIS M., 11 Lawrence Street, Chelsea
New York University College of Medicine, 1939

Robert L. Goodale, *Secretary*
330 Dartmouth Street, Boston

WORCESTER DISTRICT

- ADAMS, LAMBI N., St Vincent's Hospital, Worcester
Hahnemann Medical College, 1941
- BENNETT, NOE N., 17 Grove Street, Millbury
Tufts College Medical School, 1942
- BROWN, CHESTER W., 32 Buckley Road, Worcester
University of Rochester School of Medicine, 1939
- DEERING, GEORGE E., JR., 299 Belmont Street, Worcester
Harvard Medical School, 1943
- GOULD, MAXWELL E., 20 Goldthwait Road, Worcester
Middlesex University School of Medicine, 1938 Sponsor Ralph S. Perkins, 27 Elm Street, Worcester
- GUILD, S. ALDEN, 15 Worcester Street, Grafton
Tufts College Medical School, 1942
- JEWETT, EVERETT P., 2 Bellingham Road, Worcester
Tufts College Medical School, 1943
- KARPAWICH, PETER P., 237 Millbury Street, Worcester
Hahnemann Medical College, 1940
- KUEKAN, JAMES R., 54 Cottage Street, Whitinsville
Tufts College Medical School, 1944
- LAREAU, HENRY R., 62 Mechanic Street, Spencer
Boston University School of Medicine, 1942
- LA VIGNE, RICHARD J., 467 Chandler Street, Worcester
Tufts College Medical School, 1941
- LAVOIE, ROBERT J., 170 Dana Avenue, Worcester
Hahnemann Medical College, 1941
- PELLOCK, CHARLES J., 515 Main Street, Shrewsbury
College of Physicians and Surgeons, Boston, 1936 Sponsor Edward O. Horne, 24 Holman Street, Shrewsbury
- SCRICCO, MICHAEL W., 13 Shelby Street, Worcester
Albany Medical College, 1941
- SEIDENBERG, DANIEL, 845 Main Street, Worcester
Kansas City University of Physicians and Surgeons, 1929 Sponsor Oscar Feinsilver, 390 Main Street, Worcester
- SHANNON, MARY C., 334 Highland Street, Worcester
Kansas City University of Physicians and Surgeons, 1927 Sponsor Ernest L. Hunt, 28 Pleasant Street, Worcester
- SIKORSKY, LUCY N., 4 Oak Street, Grafton
Boston University School of Medicine, 1928

- STARR, STEVEN J., St Vincent's Hospital, Worcester
Georgetown University School of Medicine, 1941
- WOJCIECHOWSKI, ANTHONY A., 38 Crosby Street, Webster
Tufts College Medical School, 1942

Julius J. Tegelberg, *Secretary*
57 Cedar Street, Worcester

WORCESTER NORTH DISTRICT

- LAMB, MARSHALL A., 197 Central Street, Winchendon
Tufts College Medical School, 1939
- RITTENHOUSE, HARVEY L., 20 Pleasant Street, Ayer
College of Medical Evangelists, 1943

James G. Simmons, *Secretary*
30 Myrtle Avenue, Fitchburg

DEATHS

CLUTE — Howard M. Clute, M.D., of Boston, died September 19. He was in his fifty-seventh year. Dr. Clute received his degree from Dartmouth Medical School in 1914. He was professor of surgery at Boston University School of Medicine and was a member of the New England Surgical Society, the American Surgical Association and the Southern Surgical Association and a fellow of the American College of Surgeons and the American Medical Association. His widow, a son and a daughter survive.

MARSDEN — George Marsden, M.D., of New Bedford, died May 20. He was in his sixty-ninth year. Dr. Marsden received his degree from Johns Hopkins University School of Medicine in 1906. He was a fellow of the American Medical Association.

O'BRIEN — Thomas F. O'Brien, M.D., of Worcester, died September 16. He was in his fifty-first year. Dr. O'Brien received his degree from Harvard Medical School in 1921. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American College of Surgeons and the American Medical Association.

TINKHAM — Oliver G. Tinkham, M.D., of Newton, died September 10. He was in his sixty-seventh year. Dr. Tinkham received his degree from Tufts College Medical School in 1905. He was a member of the New England Obstetrical and Gynecological Society and a fellow of the American College of Surgeons and the American Medical Association. His widow and a son survive.

BOOK REVIEWS

Hayfever Plants. Their appearance, distribution and time of flowering, and their role in hayfever, with special reference to North America. By Roger P. Wodehouse, Ph.D., cloth, 245 pp., with 73 illustrations. A publication of the Chronica Botanica Company, Waltham, Massachusetts. New York City: G. E. Stechert and Company, 1945. \$4.75.

This valuable monograph brings together for the first time in one volume all the plants whose pollens cause, or are suspected of causing, hay fever. The arrangement is botanical, following the sequence of Engler and Prantl. The plants described fall into two classes — the gymnosperms, which are relatively few, and the angiosperms, which comprise the majority. Botanical and common names are used in the descriptions, which are well written and sufficient for that purpose, including the physical characteristics, distribution, time of flowering and the part the plants play in the causation of hay fever. The numerous illustrations of flowers and pollens should prove useful for identification.

The work is divided into two main parts: the first discusses pollen and pollination and the role of pollen in hay fever, and the second consists of a series of regional surveys.

overing areas in the United States, Canada and Mexico the United States is divided into ten regions, and only the noxious plants are described for each region

An interesting short chapter on the botany of hay fever, in which atmospheric pollen is considered, is found at the beginning of the book, and a selected bibliography is appended to the text.

The book is well printed with a good type on nonglare paper, with good margins

This monograph is recommended for all physicians coming into contact with allergic disturbances, as well as for all medical, public and reference libraries

Facial Prostheses By Arthur H Bulbulian, M S, D D S, 8°, cloth, 241 pp, with 202 illustrations Philadelphia W B Saunders Company, 1945 \$5 60

The reconstructive surgeon is constantly confronted with problems involving prosthetic restorations. The general surgeon in the treatment of cancer and major trauma also not infrequently has cases in which prosthetic restorations, either temporary or permanent, have much to offer. As the author plainly states, the repair of facial deformities is primarily a surgical problem, but there are numerous conditions and circumstances that make surgery impossible or inadvisable. In such a case a prosthetic device may be the answer. Prosthetic restorations of the missing parts of the extremities have long been an accepted orthopedic procedure, but surgery knows little about the possibility of prosthetic restoration of deformities of the face and jaws. One reason is that this specialty has been developed by dentists, and dental literature and subject matter are almost exclusively in dental periodicals and books. Secondly, since this is a highly specialized subject, few in the dental profession have taken the necessary training for the construction of such complicated prosthetic devices as are needed for facial and maxillary problems.

This concise book will undoubtedly fill a great demand, since at the present time there seems to be more interest in facial prosthesis than ever before. The author limits his subject, however, to the diagnosis of artificial restorations of the face, especially of the ears, nose and orbits, he does not consider maxillary restorations, which are often part of such deformities.

According to the opinion of the reviewer, the author has somewhat overemphasized the use of latex as a suitable material for restoration and has not given sufficient emphasis to other materials, such as acrylics.

The book is divided into fourteen chapters, and the classification of subjects is excellent. There are numerous diagrams and illustrations to help the reader in carrying out the technique of restoration. It is a good, small book to introduce prosthetic concepts and technique to the person interested in restorative problems of the face.

Pulmonary Tuberculosis in the Adult Its fundamental aspects By Max Pinner, M D 8°, cloth, 579 pp, with 59 illustrations and 57 graphs Springfield, Illinois Charles C Thomas, 1945 \$7 50

This book, written by a lifelong student of tuberculosis, is a treatise on clinical tuberculosis from the standpoint of the pathologist. In a protean disease like tuberculosis, with its multiple manifestations, a proper understanding of the pathophysiology and its relation to immunity and allergy is of great practical importance. In the preface — the "apologia," as the author calls it — it is stated that the main purpose of the book is not to add another text on tuberculosis or to tell the practitioner how to do this or that, but to harmonize the clinical point of view with the broad aspects of pathological, bacteriologic and immunologic facts.

Out of nineteen chapters, only four can be classed as dealing with bedside observations and treatments. The other fifteen delve deeply into such subjects as histogenesis, immunologic and phthisiogenetic principles, typical lesions of pulmonary tuberculosis, with autopsic examples, and physiologic principles of respiration, to mention only a few of the topics. These chapters reflect the viewpoint of the author, who insisted for many years that an understanding of the basic principles of pathology is the key to intelligent treatment of tuberculosis — this is not to say that he completely neglects the clinical side. Diagnostic criteria are thoroughly discussed,

and medical as well as collapse therapy is fully evaluated. The physiology of respiration and the physiologic and pathological correlations of collapse therapy receive due attention.

An added feature is the abstracted bibliography in which the articles are briefly discussed and comments and criticisms added. This should be most helpful to the reader who can at a glance obtain all the divergent points of view written in the last two or three decades.

The text is written in an easy and clear style and is illustrated by well chosen and excellently reproduced microscopic as well as radiologic pictures. It is a book for the student or the specialist of tuberculosis. It is not intended for the undergraduate or general practitioner. This volume should find a place in the library of anyone interested in any of the many phases of pulmonary tuberculosis.

The Principal Nervous Pathways Neurological charts and schemes with explanatory notes By Andrew T Rasmussen, Ph D Third edition 4°, cloth, 73 pp New York The Macmillan Company, 1945

This outstanding contribution to neuroanatomy, first published in 1932, has been revised at proper intervals. It is one of the best books on the subject and can be fully recommended. The author's position in the field is outstanding, and the book reflects his continued activity in presenting the most recent advances in neuroanatomy. In the new edition he has made definite modifications in some of the charts and minor alterations in others. When doubt exists, the author does not hesitate to query the finding, thus indicating the broad basis of his researches and always seeking a definitive point of view. The book is highly recommended.

Report of the National Health Survey Conducted by Canadian Medical Procurement and Assignment Board 8°, paper, 336 pp Ottawa Edmond Cloutier, 1945

The primary function of the Canadian Medical Procurement and Assignment Board, established in July, 1932, was to obtain physicians for the armed forces and at the same time to provide adequate medical service for the civilian population. It became apparent that the health services of the country needed to be studied, and that this involved physicians, dentists, nurses, hospitals, medical schools, public health, medical research, industrial medicine, and the communities generally. This volume is a report of that study. Although much of the report pertains to the war period, parts of it will be of use in later years. It is doubtful whether this book will be of much interest to the average practitioner of medicine, but it will be valuable to the small group interested in such problems.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Bibliography of Infantile Paralysis, 1789-1944 With selected abstracts and annotations Prepared under direction of the National Foundation for Infantile Paralysis, Inc. Edited by Morris Fishbein, M D, editor, *Journal of the American Medical Association*. Compiled by Ludvig Hektoen, M D, and Ella M Salmonsens 4°, cloth, 672 pp Philadelphia J B Lippincott Company, 1946

This selective bibliography covers the clinical and investigative work on infantile paralysis appearing in monographs, pamphlets and theses since its description by Underwood in 1789. Little or no attention is paid to textbooks, systems of medicine, encyclopedias, the official publications of boards of health and pamphlets devoted to general health education, except when representing innovations. The scientific medical literature of the last few years from foreign countries is not complete, since the material has not been easily accessible. Future supplements are planned for the purpose of remedying this defect. The material is arranged chronologically, each reference is numbered, and there are two comprehensive indexes of authors and subjects. The volume is recommended as a reference text for all medical and public-health libraries.

A Primer of Electrocardiography By George Burch, M.D., associate professor of medicine, Tulane University School of Medicine, senior visiting physician, Charity Hospital, consultant in cardiovascular diseases, Ochsner Clinic, and visiting physician, Touro Infirmary, New Orleans, and Travis Winsor, M.D., instructor in medicine, Tulane University School of Medicine, and assistant visiting physician, Charity Hospital, New Orleans 8°, cloth, 215 pp., with 235 illustrations Philadelphia Lea and Febiger, 1945 \$3 50

This primer was written to enable the student who is unfamiliar with the subject to grasp a fundamental knowledge of electrocardiography in the most direct manner. Photographs of electrocardiograms have been excluded but diagrams are literally employed to illustrate typical electrocardiographic patterns. The material is presented from a mechanistic point of view as only with the knowledge of the mechanism is it possible for the reader of electrocardiograms to unravel individual tracings. The presentation has been kept simple and brief as the work is designed to supplement the many monographs on electrocardiography that are now available

The Art of Medicine in Relation to the Progress of Thought. A lecture in the history of science course in the University of Cambridge February 10, 1945 By A. E. Clark-Kennedy, M.D., F.R.C.P., physician to the London Hospital and dean of the Medical School and fellow of Corpus Christi College, Cambridge 12°, paper, 48 pp. Cambridge, England University Press, 1945 75 cents

In this lecture Dr. Clark-Kennedy devotes most of his text to modern medicine in relation to current thought. To complete his task, however, he has made a brief review of the three periods of the past from Hippocrates to Descartes

Clinical Traumatic Surgery By John J. Moorhead, M.D., D.Sc., medical director, New York City Transit System, and consulting surgeon, Post-Graduate Hospital, United States Public Health Service, All Souls (Morristown), Anne May Memorial (Spring Lake), Caledonian, Harlem, Mary Immaculate (Jamaica), Mother Cabrini, New Rochelle, Nyack, Rockland State, St. Francis (Port Jervis) and Yonkers General hospitals 8°, cloth, 747 pp., with 500 illustrations Philadelphia W. B. Saunders Company, 1945 \$10 00

This book has been written with the main idea of placing in one volume all the information necessary to diagnose the usual and most of the unusual effects of accident and injury. The author has summed up his two-score years of active experience in the field and has drawn on the subject matter of his teaching courses at postgraduate medical schools. The work is well printed on good paper but is rather heavy for its size

Government in Public Health By Harry S. Mustard, M.D., LL.D., DeLamar Professor of Public Health Practice, and director, School of Public Health, Faculty of Medicine, Columbia University 8°, cloth, 219 pp., with 11 tables New York The Commonwealth Fund, 1945 \$1 50

Dr. Mustard in this monograph brings out the rapid extension of the field of public health as one of the important trends in modern medicine. He traces the development of state health departments and describes their proper sphere of action. The volume is issued as one of the series published under the auspices of the Committee on Medicine and the Changing Order of the New York Academy of Medicine

One Hundred Years of Gynaecology, 1800-1900. A comprehensive review of the specialty during its greatest century, with summaries and case reports of all diseases pertaining to women. By James V. Ricci, M.D., clinical professor of gynecology and obstetrics, New York Medical College, director of gynecology of the City Hospital, New York, director of gynecology and obstetrics, Columbus Hospital, attending gynecologist and obstetrician, Flower and Fifth Avenue hospitals, New York, and consultant in gynecology and obstetrics, Downtown Hospital, New York 4°, cloth, 651 pp. Philadelphia The Blakiston Company, 1945 \$8 50

The author has attempted to survey the gynecologic literature of the nineteenth century and in conjunction with his previous volume, *The Genealogy of Gynaecology* (1943), provides a history of the subject from 2000 B.C. to 1900 A.D. This work should prove of value as a reference text and should be in all medical libraries

NOTICES

ANNOUNCEMENTS

Dr. Charles Bushold, having returned from the armed services, is resuming practice at 351 Essex Street, Lawrence.

Dr. Henry M. Gahan announces his return from military service and resumption of practice at 19 Washington Street, Medford

Dr. Louis Nathan, having returned from military service, is resuming practice at 276 Commonwealth Avenue, Boston.

EXHIBITION IN COMMEMORATION OF ETHER CENTENARY

The Boston Medical Library, in conjunction with the Boston Public Library and the Massachusetts Historical Society, will hold an exhibition in commemoration of the Ether Centenary, in the Treasure Room of the Boston Public Library, from October 15 to December 15

The material exhibited will occupy all the cases in the Treasure Room and will cover the period from the beginnings of anesthesia, about 4000 B.C., to 1846. Emphasis will be placed on the work of Dr. William T. G. Morton

AMERICAN ACADEMY OF ALLERGY

The American Academy of Allergy will hold its annual convention at the Hotel Pennsylvania, New York City, from November 25 to 27 inclusive. All physicians interested in allergic problems are cordially invited to attend the sessions as guests of the Academy without payment of registration fee. The program has been arranged to cover a wide variety of conditions in which allergic factors may be important. Papers will be presented dealing with the latest methods of diagnosis and treatment as well as the results of investigation and research. Advance copies of the program may be obtained by writing to Dr. Horace S. Baldwin, chairman on arrangements, 136 East 64th Street, New York City, prior to November 10

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

The first postwar meeting of the American Academy of Dermatology and Syphilology will be held at the Hotel Statler, Cleveland, Ohio, from December 7 to 12 inclusive, with daily symposiums at the Allerton Hotel and teaching clinics at the Cleveland City Hospital. Dr. Howard M. Cole, of Cleveland, will be in charge of local arrangements

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 17

FRIDAY OCTOBER 18

*9 00-10 00 a.m. Recent Studies in Hemorrhagic Shock Dr. Arnold M. Selegman Joseph H. Pratt Diagnostic Hospital.

*10 00 a.m.-12 00 m. Medical Staff Rounds, Peter Bent Brigham Hospital

MONDAY OCTOBER 21

*12 15-1 15 p.m. Chalcopathological Conference Peter Bent Brigham Hospital

(Notices continued on page xviii)

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ENTERIC INFECTIONS AND THEIR SEQUELAE*

ROGER A. LEWIS, M.D.†

BOSTON

THE acute dysenteric diseases have been studied in various overseas installations throughout the world, but follow-up studies are scarce. Most of the patients in this group were carefully observed overseas, and in many cases the complete clinical record was available, making the follow-up study particularly significant. The cases referred to below were observed on the gastrointestinal section of a United States Army general hospital during the latter half of 1945. Attention was centered on the problems of diagnosis and treatment, since little importance could be attached to incidence in such a selected group of cases.

Overseas records and routine case histories were supplemented by systematic interviews that could be charted in tabular form. All the patients were allowed home for thirty to sixty days before final checkup, to provide a sufficiently long follow-up period after treatment, and practically all were examined with a sigmoidoscope. The laboratory study included at least six stool examinations, one specimen being obtained from sigmoid washings and one after purgation. Stool cultures were supplemented by rectal cultures. When steatorrhea was suspected a twenty-four-hour stool was collected for further observation.

An over-all picture of the cases studied is presented in Table 1, which lists the diagnoses made overseas and in the United States. Amebiasis was diagnosed in over a fourth of the cases. The number of patients diagnosed as carriers of *Endamoeba histolytica* was larger in the United States than overseas. The incidence of hookworm infestation was identical, with as many new cases as old ones that had been cleared of parasites. More patients were found to have strongyloidiasis in the United States than overseas. No new cases of schistosomiasis were discovered, and in several of the old cases negative stools were observed in the United States, where there was a marked increase in the number of diag-

noses of such sequelae of intestinal disease as colitis, chronic diarrhea and steatorrhea.

Of the 105 men in this group, only 2 had never been overseas, 11 had served in the European Theater of Operations, and 92 had been in the Pacific, including the China and India-Burma theaters. Many of those from the Pacific had served in several areas, and a considerable number had no symptoms until they returned to the United States. Some patients had no symptoms of enteric disease and no pathological findings other than eosinophilia and ova in the stools. Such patients are referred to

TABLE 1 Summary of Enteric Diseases

DISEASE	CASES DIAGNOSED OVERSEAS	CASES DIAGNOSED IN THE UNITED STATES		
		ACTIVE CASES	CARRIERS	TOTAL CASES
Ankylostomiasis	29	0	32	32
Amebic dysentery	37	28	15	43
Amebic hepatitis	3	2	0	2
Amebic liver abscess	3	2	0	2
Schistosomiasis	15	7	1	8
Strongyloidiasis	10	10	5	15
Ascariasis	6	1	4	5
Bacillary dysentery	5	0	1	1
Unclassified dysentery	9	1	0	1
Steatorrhea	1	7	0	7
Chronic diarrhea	0	11	0	11
Ulcerative colitis	2	4	0	4
Rectal granuloma	0	3	0	3
Mucous colitis	0	2	0	2
Rectal stricture	1	1	0	1
Appendiceal cyst	0	1	0	1
Totals	124	80	53	138

below as carriers. In Table 1 the infestations that were diagnosed in the United States are divided into active and carrier cases. With hookworm and ascariasis infestation the number of carriers far exceeded those with symptoms. In amebiasis, strongyloidiasis and schistosomiasis there were more patients with symptoms than there were carriers. Patients with active cases were admitted to the ward for obvious reasons, whereas carriers were found through routine examination or because of stool studies ordered after eosinophilia had been noted.

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In this group of patients the average duration of illness before arrival in the United States was six months, and the average length of hospital stay in the United States was three months. The latent period from exposure to illness varied from one to twenty-four months. Of the entire group of 105 men only a fourth were discharged from the section as fit for full duty.

CARRIERS OF *Endamoeba Histolytica*

A carrier of *E. histolytica* is by definition a person who harbors the organism without having signs or symptoms of disease that might be associated with this infestation. It is well known that when the stool is solid the amebas are usually encysted and

amebic treatment. The last man developed typical amebic dysentery and was found to have trophozoites. Thus, in the 5 cases, 4 patients were eventually treated.

At first, carriers of *E. histolytica* were treated according to the conventional routine described below, Diiodoquin being used instead of chiniofon because of the high incidence of diarrhea with the latter.¹ Nevertheless, 20 per cent of the carriers developed diarrhea with carbarsone. Subsequently carrier cases were treated with vioform alone.

AMEBIC DYSENTERY

In this group of men a diagnosis of amebic dysentery was made overseas in 30 cases and in the United

TABLE 2 Final Results of Treatment in 5 Carrier Cases of *Endamoeba Histolytica* Diagnosed in the Pacific Theater and Followed in the United States

CASE No.	HISTORY OF DIARRHEA	OTHER DISEASE	FINDINGS OVERSEAS	TREATMENT OVERSEAS	SYMPTOMS IN UNITED STATES	FINDINGS IN UNITED STATES	TREATMENT IN UNITED STATES
1	Yes	Hepatitis	Cysts	None	None	None	None
2	Yes	Hepatitis and schistosomiasis	Cysts	Maparsen and fuadin	None	Cysts	Carbarsone and Diiodoquin
3	Yes	Schistosomiasis	Trophozoites	Sulfaguanidine and fuadin	None	Trophozoites	Carbarsone, Diiodoquin and emetine
4	Yes	Schistosomiasis	Trophozoites	Fuadin	Diarrhea	Trophozoites	Carbarsone, Diiodoquin and emetine
5	Yes	Hepatitis	Trophozoites	None	Diarrhea	None	Vioform

that when the stool is liquid for any reason the organisms are usually motile. Of the 15 patients diagnosed as carriers in the United States 64 per cent harbored cysts, 30 per cent harbored trophozoites and 6 per cent showed both cysts and trophozoites. Most of these patients were under investigation for

States in 20. Most of the cases were contracted in or after exposure in the Pacific Theater. A few patients came from the China and India-Burma theaters, and a few from the European Theater, despite the disproportion in the number of troops exposed. There was a latent period of at least one to

TABLE 3 Severity of Attacks of Amebic Dysentery as Indicated by Associated Findings

OCCURRENCE OF ATTACK	TOTAL No OF PATIENTS*	TROPHOZOITES	CYSTS	DIARRHEA	WATERY STOOLS	BLOODY STOOLS	ULCERATION	RELAPSES	OTHER COMPLICATIONS	DRUG REACTIONS
		%	%	%	%	%	%	%	%	%
Overseas	30	83	17	97	93	50	59	40	60	10
In the United States	20	80	25	75	55	15	25	5	10	0

*Enemas were administered to 13 per cent of patients overseas and to 25 per cent of patients in the United States.

some other disease, and amebas were found during routine stool examinations. In 1 case the organisms were discovered in a purged stool sent to the laboratory after administration of a vermifuge.

The final results in the 5 carrier cases of *E. histolytica* that were found overseas are summarized in Table 2. These men were not given antiamebic treatment overseas because of the presence of more serious disease. One man, nevertheless, remained symptom free, and amebas were not found in the stools. Another remained asymptomatic but was found to harbor cysts. Another remained asymptomatic but was found to harbor trophozoites. One patient developed diarrhea that subsided after anti-

nine months from exposure until onset of the disease in the 20 cases diagnosed in the United States.

Although most of the patients with amebic dysentery were found to harbor trophozoites, cysts were discovered in a significant number (Table 3). In 3 cases the diagnosis was not established until a purged stool specimen was obtained, and in 2 the first positive specimen was obtained from sigmoid washings. Of the 20 cases in the United States complement-fixation tests were positive in only 7 (Table 4). Six cases were severe, 5 leading to ulceration and 1 being accompanied by hepatitis. In none of the 20 carrier cases diagnosed in the United States was the complement-fixation test positive. Con-

trary to the experience of others,² the test was of no value in picking up cases of intestinal amebiasis

Attacks of amebic dysentery in persons returning from overseas were less severe than those occurring overseas but severer than similar infections acquired in the United States. The overseas attacks were almost invariably accompanied by severe diarrhea and the incidence of ulceration was high (Table 3). The overseas recurrence rate of over 40 per cent

scuss, 2 of appendicitis and 1 of mucous colitis. Of the patients who had amebic dysentery in the United States 1 was found to have granuloma and another developed chronic diarrhea. The disproportion in the number of complications in the two groups may have been due to several factors. In the first place, it was chiefly patients with complicated cases that were returned to the United States. Secondly, the overseas attacks were severer. Finally, thorough

TABLE 4 Cases of Amebic Dysentery with Positive Complement-Fixation Tests

DATE OF POSITIVE STOOL EXAMINATION	DATE OF TREATMENT	DATE OF POSITIVE COMPLEMENT-FIXATION TEST	REMARKS AND COMPLICATIONS
April 20 1945	April 30 1945	—	Two attacks of dysentery with rectal stricture
May 24, 1945	July 1, 1945	July 7 1945	Eight attacks of dysentery with ulceration
September 1944	September, 1945	—	Two attacks of dysentery, with ulceration
July 22 1945	August 1 1945	July 7 1945	Probably 2 attacks of dysentery with ulceration
March 22 1945	March 28, 1945	—	Ulceration and ulcerative colitis
August 3, 1945	August 16 1945	August 7 1945	Amebic hepatitis and dysentery
—	February 22 1945	—	Chronic dysentery (since 1944) with ulceration
May 31 1945	August 16, 1945	July 31 1945	
February 18 1945	February 22 1945	—	
—	June 20 1945	July 31 1945	
May 29 1945	May 13 1945	—	
June 23 1945	June 8, 1945	August 7 1945	
—	—	—	
August 21, 1945	August 22 1945	August 21 1945	

contrasts with that of 5 per cent in the United States and may partly have been due to the fact that with one exception patients overseas were not given retention enemas in the treatment of the first attack (Table 3).

Most of the overseas attacks of amebic dysentery were treated with approximately a week of emetine, carbarsone and chiniofon. In Table 5 the treatment

treatment with retention enemas may have prevented some of the complications of amebic dysentery.

Diarrhea following the administration of chiniofon and carbarsone was mentioned above. Another minor toxic effect—vomiting after the injection of emetine—can be obviated by the use of divided doses. Severer toxic reactions to emetine were noted

TABLE 5 Data in 6 Cases of Amebic Dysentery Diagnosed Overseas with Relapse in the United States

TREATMENT	COMPLICATIONS	COURSES OF EMETINE	COURSES OF ORAL CARBARSONE	COURSES OF ORAL CHINIOFON	COURSES OF ORAL DIODIOQUIN	NO OF CARBARSONE ENEMAS
China and India-Burma	Diarrhea watery and bloody stools and ulceration	4	7	2	5	1
Pacific	Diarrhea watery stools and ulceration	0	1	1	1	0
Pacific	Diarrhea watery and bloody stools and ulceration	1	2	0	2	0
Pacific	Diarrhea	1	1	0	0	0
Pacific	Diarrhea, watery and bloody stools and ulceration	1	1	1	0	0
Pacific	Diarrhea, watery and bloody stools and ulceration	3	3	0	3	2

is summarized for the 6 patients who had amebic dysentery overseas with relapse in the United States. This table emphasizes the fact that although most of the overseas cases were accompanied by ulceration few patients received retention enemas. In the United States 25 per cent of the men were found to have ulceration and practically all received enemas.

Of the patients who had amebic dysentery overseas 57 per cent developed complications, including 4 cases of ulcerative colitis, 3 of granuloma, 3 of chronic diarrhea, 2 of steatorrhea, 2 of amebic ab-

when injections had been continued for more than seven days or resumed without an adequate rest period. These reactions consisted of localized palsies. In 1 case an abscess of the deltoid muscle followed emetine injections. One man developed exfoliative dermatitis and hepatitis following carbarsone and gave a history of a similar reaction following neosarsphenamine.

AMEBIC HEPATITIS AND AMEBIC ABSCESS

In this group of 105 men 10 had a total of twelve attacks of amebic hepatitis or abscess, not including

cases of hepatomegaly during the course of typical amebic dysentery. Eight of the attacks occurred overseas, and 4 in the United States. All the men had been in the Pacific, China or India-Burma Theater. The diagnostic factors in these cases are summarized in Table 6.

Prompt diagnosis and treatment of amebic hepatitis may prevent the development of abscess formation, and even after the abscess has occurred treatment may cause resolution without operation or drainage. Of the 8 overseas attacks, at least 5 went on to abscess formation, 4 being drained surgically and 1 by spontaneous rupture into a bronchus. Of

tion relapsed, 1 with amebic dysentery and 2 with amebic abscess of the liver, whereas the patients given adequate medication did not relapse. Although oral treatment may be deferred until after the course of emetine has been completed, it should not be overlooked when the patient becomes asymptomatic, because the effect of emetine on intestinal amebiasis is only temporary.

AMEBIC APPENDICITIS, GRANULOMA AND RECTAL STRICTURE

The incidence of involvement of the appendix in amebic dysentery has been pointed out.³ In 3

TABLE 6 Data in 10 Cases of Amebic Abscess and Hepatitis

Occurrence of Attack Overseas	History of Diarrhea	Maximum Temperature °F	Tenderness over Liver	Icteric Index	White Cell Count X 10 ³	Fixation of Diaphragm	Pulmonary Infiltration	Complement-Fixation Test	Source of <i>E. histolytica</i>	Liver Abscess	Rupture or Drainage of Liver Abscess	Emetine Injections days	Full Dose of Carbarsone days	Diodoquin Chloroquin or Vioborn days	Relapse or Complication
Overseas	No	101	Yes	—	7	No	No	Positive	Pus	Yes	Yes	0	0	0	Amebic abscess
In the United States	No	103	Yes	—	16	No	No	Positive	None	Yes	No	6	0	10	None
In the United States	Yes	99	Yes	—	14	No	No	Negative	None	No	No	6	0	20	None
Overseas	Yes	104	Yes	—	16	No	No	Positive	None	Yes	Yes	0	0	0	Amebic dysentery
In the United States	Yes	100	Yes	—	9	No	No	Negative	None	No	No	6	0	10	None
Overseas	Yes	103	Yes	—	15	Yes	Yes	—	Stool	Yes	No	6	0	7	None
Overseas	Yes	101	Yes	—	22	Yes	Yes	Negative	Sputum	Yes	Yes	10	0	0	Amebic abscess
In the United States	Yes	100	Yes	40	10	Yes	No	Negative	None	Yes	No	8	7	7	None
Overseas	Yes	102	Yes	13	18	No	No	Positive	None	No	No	10	30	20	None
Overseas	Yes	103	Yes	—	22	Yes	Yes	—	Stool	Yes	Yes	7	7	7	None
Overseas	Yes	102	Yes	—	5	No	No	Positive	Stool	No	No	7	7	7	None
Overseas	Yes	104	Yes	—	12	Yes	No	Positive	Stool	No	No	10	6	0	None

the 4 cases diagnosed in the United States 2 went on to abscess formation but resolution occurred without drainage. The chief factors in the early diagnosis of amebic hepatitis and abscess are tenderness and enlargement of the liver, with varying degrees of fever and leukocytosis usually without jaundice and often without amebas in the stools. In addition to fixation of the diaphragm there may be x-ray evidence of pulmonary infiltration, consequently, several patients were treated for pneumonia before amebiasis was suspected. The complement-fixation test, which is often positive in amebic hepatitis, may persist long after successful treatment. It is hazardous to wait for laboratory confirmation in dealing with amebic abscess or hepatitis, and the therapeutic response to emetine is sufficiently dramatic to aid in establishing the diagnosis.

The necessity of treating amebic abscess and hepatitis with either carbarsone or one of the iodine containing oxyquinolines is shown clearly in Table 6. The 3 patients treated without adequate oral medica-

tion relapsed, 1 with amebic dysentery and 2 with amebic abscess of the liver, whereas the patients given adequate medication did not relapse. Although oral treatment may be deferred until after the course of emetine has been completed, it should not be overlooked when the patient becomes asymptomatic, because the effect of emetine on intestinal amebiasis is only temporary.

In 3 patients who had amebic dysentery overseas, granulomatous lesions were found on proctoscopic examination in the United States. One man had diarrhea for four months before antiamebic treatment was given, the lesions disappeared after a course of Diodoquin retention enemas. Another patient, who had had several recurrences of amebic dysentery, developed similar lesions, which cleared up when the stools became negative. A patient who did not receive antiamebic therapy until late in the

se of the disease developed ulcerative colitis and survival in the United States had only a few granulosus lesions that cleared up without further specific therapy. It is interesting to note that at time of discharge these patients were still subject to recurrent attacks of mild diarrhea brought on by stress or food indiscretion.

Stricture of the rectum occurred in 1 patient who had severe dysentery with amebiasis discovered after an appendectomy had been performed. Despite several courses of emetine and oral carbarsone he developed stricture of the rectum. The complement-

are visible the use of chiniofon or carbarsone retention enemas is also recommended. In amebic abscess and hepatitis the emetine is prolonged for a total of eight days, and carbarsone is omitted. This regime, although it was followed closely overseas, led to a relapse rate of 40 per cent in this selected group of cases. Furthermore, diarrhea medication was frequently noted, especially with chiniofon but also with carbarsone.

Recent studies of blood iodine levels suggest that vioform is the best of the available iodine-containing derivatives of oxyquinoline.⁴ Unfortunately,

TABLE 7 Schedules for the Treatment of Amebiasis

TYPE OF CASE	CONVENTIONAL SCHEDULE			SIMPLIFIED SCHEDULE		
	DRUG USED	DOSE gm	PERIOD days	DRUG USED	DOSE gm	PERIOD days
Carrier	Carbarsone Chiniofon or Diodoquin	0.75 1.00 1.80	7 7 7	Vioform	1.00	10
Mild amebic dysentery	Carbarsone Chiniofon or Diodoquin	0.75 3.00 1.80	7 7 7	Emetine Vioform	0.06 1.00	6 10
Acute or chronic amebic dysentery	Emetine Carbarsone Chiniofon or Diodoquin	0.06 0.75 3.00 1.80	6 7 7 7	Emetine Vioform Vioform coemas	0.06 1.00 2.00	6 10 5
Severe amebic dysentery	Emetine Carbarsone Chiniofon or Diodoquin Chiniofon enemas or Carbarsone enemas	0.06 0.75 3.00 1.80 4.00 2.00	6 7 7 7 5 5	Emetine Vioform Vioform coemas	0.06 1.00 2.00	6 10 5
Amebic abscess or hepatitis	Emetine Chiniofon Diodoquin	0.06 0.75 1.80	8 7 7	Emetine Vioform	0.06 1.00	8 10

ation test was positive. The weight fell from 205 to 30 pounds, and the patient died after a colostomy.

ANTIAMEBIC DRUGS

The sulfanilamide derivatives are mentioned because they are frequently prescribed in the treatment of dysentery of unknown origin. Sulfadiazine or sulfaguanidine was given to 15 men in this series who were subsequently found to have amebiasis. Although in some cases the original illness may have been bacillary dysentery that provoked or was followed by amebic dysentery, in others it is likely that the sulfanilamide derivatives caused a temporary improvement in the amebic infection. Most of the patients with undiagnosed dysentery treated with the sulfonamides relapsed with typical amebic dysentery — 1 with amebic hepatitis.

The conventional schedule for the treatment of amebiasis is based on a combination of three different types of drugs — emetine, carbarsone and iodine containing oxyquinoline (Table 7). Carriers and patients with mild enteric symptoms were given 0.75 gm of carbarsone daily for a week, followed by 3.0 gm of chiniofon or 1.8 gm of Diodoquin daily for another week. Patients with acute and chronic cases of amebic dysentery were given the same treatment, with the addition of 0.06 gm of emetine daily for six days. In refractory cases and when ulcers

nately, an erroneous statement in the literature that vioform is irritating when given rectally⁵ has been repeated in textbooks and has deterred physicians from employing retention enemas of vioform or Diodoquin. This report was incorrectly based on a previously reported experiment in which the hydrochloric acid derivative of vioform was used.⁶ Vioform is now available in a powdered form that makes an excellent suspension in tap water and is not irritating even when given to patients with severe amebic or ulcerative colitis. Diodoquin, which is also nonirritating, must be powdered before it can be suspended in water. When vioform is used rectally 200 cc of a 1 per cent suspension is given on alternate nights for five doses.

With a knowledge of the chemical stability and nonirritating properties of vioform a new schedule of treatment has been devised (Table 7). This schedule calls for 1.0 gm of vioform daily for ten days, instead of both carbarsone and chiniofon. Emetine is given in all symptomatic cases, and retention enemas of vioform are given concurrently with the oral course of this drug in all but the mildest cases of amebic infection. This schedule of treatment has been effective in the most resistant cases of amebic dysentery, including those from the India-Burma Theater, and has abolished diarrhea medication (Table 8).

ULCERATIVE COLITIS

Five patients in this series were admitted to the hospital with a diagnosis of ulcerative colitis. Four had served overseas in the Pacific Theater, and 1 had never been outside the United States.

One patient gave a history of both amebic and bacillary dysentery, 3 gave a history of amebic dysentery without any known bacillary dysentery, and the patient who had not been overseas gave a history of undiagnosed dysentery acquired during an epidemic.

Three of the cases that occurred after amebic dysentery were extremely mild, and 1 was severe.

TABLE 8 *Incidence of Diarrhea with Antamebic Drugs Used in the United States*

DRUG	ROUTE	NO OF CASES	NO OF CASES WITH DIARRHEA
Chiniofon	Oral	3	2
Carbarsone	Rectal	4	1
Carbarsone	Oral	32	4
Diodoquin	Rectal	2	0
Diodoquin	Oral	36	0
Vioform	Rectal	4	0
Vioform	Oral	12	0

The other case, although not severe, had relapsed several times.

These men were all given a course of sulfadiazine, and 3 of them were also given a course of vioform. Four patients recovered, and 1 who failed to improve was transferred to another hospital.

CHRONIC DIARRHEA

The term chronic diarrhea is used to describe a condition that does not fit any other clinical syndrome. The condition, which is characterized by recurrent, self-limited attacks of mild diarrhea, is usually brought on by exercise, spiced foods or alcoholic beverages. It does not include ulcerative colitis, mucous colitis or patients with psychiatric disorders. The final diagnosis was chronic diarrhea in 10 cases in this series. Actually the incidence of this condition was greater, but when a diagnosis of amebic dysentery was made in the United States the recurrent diarrhea was considered a residual symptom of amebic infection and a diagnosis of chronic diarrhea was not made. This syndrome was also noted among persons on the hospital staff who had been overseas and had been evacuated to this country under the rotation policy.

Most of the men with chronic diarrhea had served in the Pacific, China or India-Burma Theater. All had a history of intestinal disease, and in 80 per cent a definite diagnosis of amebic dysentery had been made. One of the men suffering from chronic diarrhea had been infected with strongyloides and developed diarrhea when he was given gentian violet. In some cases the diarrhea was aggravated by treatment with carbarsone. About half the men had

hookworm infestation, and some had received several courses of tetrachlorethylene. Other, visible factors in the production of this syndrome included exposure to the hardships and food of overseas installations, especially in the zone. In these cases the diarrhea was often accompanied by cramps and a feeling of malaise that cleared up when the attack subsided. There was usually relatively slight weight loss. Physical examination was not remarkable except for tenderness over the colon or small intestine. Laboratory studies were entirely negative, including x-ray examination of the gastrointestinal tract, twenty-four-hour stool fat analysis, microscopic examination of the stool and repeated rectal cultures.

Most of the patients with chronic diarrhea were not given any specific therapy and showed gradual improvement with rest and diet. Sulfadiazine was tried in a few cases without benefit. Vioform, which caused considerable improvement in the 2 cases in which it was given, deserves further trial when the history is of amebic infection.

STEATORRHEA

Most studies of fat excretion have been based on a chemical partition of the dried stool. It is known that 5 to 10 per cent of ingested fat is excreted, but

TABLE 9 *Approximate Total Fat Excretion in Twenty-Four Hours on a Diet of 100 Gm. or Less of Fat*

CLINICAL DIAGNOSIS	WEIGHT OF STOOL gm.	PERCENTAGE OF FAT	FAT EXCRETED gm.
Pancreatogenous steatorrhea	866	9.2	80
Sprue	1949	3.7	74
Sprue	1050	4.5	47
Sprue	298	12.1	36
Sprue	522	6.0	31
Sprue	1004	1.8	18
Sprue	671	2.4	16
Ulcerative colitis	712	2.2	16
Sprue	412	2.9	12
Sprue (convalescent)	278	3.3	9
Cholecystitis (convalescent)	315	2.6	8
Chronic diarrhea	249	2.8	7
Chronic diarrhea	176	3.8	6
Malocclusion	363	1.6	6
Diarrhea from carbarsone	242	2.2	5
Amebic dysentery	253	1.4	5
Chronic diarrhea	563	0.8	5
Ulcerative colitis	170	2.8	5
Mucous colitis	270	1.5	4
Mucous colitis	223	1.8	4
Chronic diarrhea	192	1.8	3
Normal control	302	1.1	3
Chronic diarrhea	110	2.2	2
Normal control	85	1.5	1
Normal control	44	2.6	1
Malocclusion	52	2.0	1
Mucous colitis			

ever, so that with a normal intake of 100 gm. of fat the twenty-four-hour stool should not contain more than 10 gm. of fat.⁷ It is also known that diarrhea of any type may cause an increase in fat excretion but that more marked disturbances occur in pancreatic disease and sprue. For the purposes of this study a twenty-four-hour stool specimen was deemed adequate because of the presence of diarrhea. An aliquot of the moist stool was analyzed for total fat by the Fowweather method.⁸

the total fat excretion in twenty-four hours measured in 26 cases (Table 9). Normal persons excreted 1 to 5 gm. Patients with mild diarrhea excreted 3 to 9 gm. There were 9 patients who excreted 12 to 80 gm., including 1 with ulcerative colitis, 1 with pancreatogenous steatorrhea and 7 with a syndrome closely resembling tropical sprue.

Pancreatogenous diarrhea may be differentiated from sprue by several laboratory tests. In sprue the stool is bulky, there may be a lowering of the serum calcium and phosphorus, as well as the hemoglobin, and the glucose-tolerance test tends to be flat. In pancreatic disease the stool contains undigested fat particles and an increased amount of nitrogen, there may be an increase in the serum amylase, and the glucose-tolerance test may be elevated. The only case of pancreatogenous steatorrhea in this series showed all the abnormalities mentioned.

SPRUE

One of the characteristic features of sprue is that it occurs at a variable period after a person has left the tropics.⁹ It seems quite likely that steatorrhea begins long before the development of classic sprue, since it takes some time to deplete the mineral and vitamin stores. This intermediate stage in the development of sprue has been called presprue or incomplete sprue.¹⁰ Of the 7 cases in this study only 3 were diagnosed overseas.

The case histories showed several common characteristics (Table 10). All the men had served in New Guinea or the Philippines. The latter location is a well known source of a spruelike disease that has been considered a complication of amebiasis.¹¹ The period of exposure in the tropics varied from one to three years. All the men gave a history of dysentery, and amebic infection was proved in 2 cases. The average weight loss amounted to 47 pounds.

Associated with the weight loss these patients showed wasting of the musculature, looseness of the skin and marked pallor. Transient soreness and redness of the tongue in 5 of the 7 men went on to ulceration in a few cases. Gaseous distention and abdominal tenderness were frequently noted. Proctoscopic examination showed hyperemia in 4 cases. X-ray studies disclosed redundancy of the colon in 3. One man developed a peripheral neuritis.

The total bulk of the twenty-four-hour stool was markedly increased, with an average weight of 850 gm. The stool was light in color and varied from soft to liquid, with a tendency to adhere to the glass container. The total fat excretion was markedly increased, averaging 36 gm.

Gastric analysis revealed the presence of a variable amount of free acid in all cases. The serum proteins were normal or slightly less than normal. In a few cases the blood calcium and phosphorus were below normal. The average red-cell count was 4,200,000,

and the average hemoglobin 12.5 gm. The glucose-tolerance test showed a marked tendency to be low and flat, the average maximum value after 100 gm of glucose was only 115 mg per 100 cc.

Of the 2 patients in whom a diagnosis of sprue was made overseas only 1 was given a low-fat diet and liver extract. This man showed marked improvement and was convalescent when he arrived in the United States. The other patients were in poor condition, despite the fact that some of them had learned to avoid fatty food.

In the United States the patients were put on a strict low-fat diet. The regular hospital diet contained 100 gm of fat, the high-calorie diet 150 gm, and the strict low-fat diet only 40 gm. In this diet the rest of the calories were furnished by 400 gm of carbohydrate and 120 gm of protein. In addition to the diet, each patient was given 5 cc of crude liver extract twice weekly. On this regime the diarrhea improved, the cramping ceased, and there was a rapid weight gain. It was not possible to follow all these patients, but 4 were well enough to be discharged from the hospital, 2 were sent to convalescent hospitals and 1 was transferred to another general hospital.

Although the eventual prognosis in these cases cannot be determined, it is possible that the development of classic sprue was prevented by early treatment of the underlying metabolic disturbance, that is, steatorrhea.

HOOKWORM INFESTATION

Of the 45 cases of hookworm infestation in this series 13 were diagnosed overseas only, 16 were diagnosed overseas and in the United States, and 28 were diagnosed for the first time in the United States. Almost all the men were exposed in the Pacific Theater. These figures do not give a fair picture of the incidence of infestation, however, because the entire group was specially selected from the enteric disease ward.

None of the men observed in the United States had symptoms that could be ascribed to hookworm infestation. There is no doubt that symptomatic hookworm disease was encountered overseas, but sufficient treatment was given to clear the symptoms before the patients returned to the United States.

In the cases that were diagnosed overseas and were not complicated by other parasites, the average eosinophil count was 16 per cent. When these men arrived in the United States those with negative stool findings had an average eosinophil count of 2 per cent, and those with positive stool findings had an average eosinophil count of 13 per cent. In cases diagnosed in the United States for the first time the average eosinophil count was 9 per cent. The total white-cell count was sometimes increased, the maximum noted in this series being 18,000.

Overseas the treatment for hookworm infestation consisted almost entirely of tetrachlorethylene in doses of 3 cc. In some cases the drug was given in larger doses, and in some, hexylresorcinol was employed.

The results of hookworm treatment are shown in Table 11. About half the men treated overseas were found to have negative stools, and about half were found to have positive stools when they arrived in the United States, regardless of the number of treatments that had been given. Treatment in the United States gave similar results, even when the dose of tetrachlorethylene was increased to 4 cc. and 1 cc. of oil of chenopodium was added.

Although tetrachlorethylene was no more effective in the United States than overseas, few patients received more than two courses of the drug even when

tions that preceded the first positive findings may have been associated with the incubation period. The patient, who was overseas in April and May, returned in June with a white-cell count of 14,000, with 43 per cent eosinophils. Repeated stool examinations were negative until the middle of July, when larvae of strongyloides were found.

Only 5 of the 16 patients with strongyloidiasis were asymptomatic (Table 12). Eleven men complained of cramps, and 5 were also troubled with diarrhea. Tenderness on abdominal palpation was a frequent finding.

It is interesting to note that the patient was cured in only 1 of the 10 cases discovered overseas. This may in part have been due to the fact that enteric coated gentian violet was not generally available outside this country. Of the patients treated in the

TABLE 10 *Data in 6 Cases of Sprue Contracted in the Pacific Theater*

OVERSEAS SERVICE	CHIEF SYMPTOMS OVERSEAS	CHIEF TREATMENT OVERSEAS	TRANSFER DIAGNOSIS OVERSEAS	CONDITION OF TONGUE	PROCTOSCOPIC EXAMINATION	BARIUM-ENEMA EXAMINATION
mo						
16	Diarrhea and vomiting	Antiamoebic and dietary	Dysentery (unclassified)	Atrophic	Negative	Redundant colon
34	Diarrhea and vomiting	Transfusion and vitamins	Malnutrition and anemia	Sore and reddened	Negative	Negative
23	Diarrhea and vomiting	Sulfonamides	Dermatitis	Sore and reddened	Hyperemia of mucosa	Negative
27	Cramps and vomiting	Dietary	Sprue	Red and ulcerated	Hyperemia of mucosa	Redundant colon
25	Diarrhea and vomiting	Antiamoebic	Dysentery (unclassified)	Normal	Previous ulceration	Negative
15	Diarrhea and cramps	Antiamoebic and sulfonamides	Amoebic dysentery	Sore and reddened	Hyperemia of mucosa	Negative
22	Diarrhea and cramps	Dietary	Sprue	Sore and reddened	Hyperemia of mucosa	Redundant colon

the stools remained positive, and some patients were not held in the hospital long enough to determine whether ova were still being excreted. This indicates that the policy on the gastrointestinal ward was to limit retreatment to one course of tetrachlorethylene. Inasmuch as hookworm infestation is self-limited, this policy was considered safe and in fact beneficial to the patient.

STRONGYLOIDIASIS

Strongyloidiasis was found in 12 men from the Pacific Theater, in 2 from the China and India-Burma theaters and in 2 from the European Theater. Most of the diagnoses were made from routine stool examinations, but some were arrived at only after repeated studies made to find the cause of eosinophilia. In 1 case the long series of negative examina-

United States, however, at least 2 still had positive stool findings at the time of discharge. One of these men had received intravenous and intraduodenal gentian violet, as well as a thirty-day course of the oral preparation.

The situation is further complicated by the fact that strongyloidiasis is a self-perpetuating organism.¹² The need for further observation and study of this disease is obvious.

BACILLARY DYSENTERY

No patients with active cases of bacillary dysentery were admitted to the hospital in the United States during the course of these studies. One carrier of *Shigella* organisms was found who had had bacillary dysentery while in the Pacific Theater.

the other patients in this series had bacillary enteric overseas, but stool and rectal cultures were negative in the United States. One of the men who had had bacillary dysentery, however, developed mucous colitis, and another had had both bacillary and amebic dysentery developed ulcerative colitis. There were no other cases of enteric disease following bacillary dysentery, despite its widespread occurrence overseas.

MISCELLANEOUS PARASITES

Five proved cases of schistosomiasis are included in this series because of concomitant amebiasis. Four of these patients were found to have ova in the stools both overseas and in the United States, whereas stool examinations in 2 cases were positive overseas.

There were several asymptomatic carriers of *Trichuris trichura*, *Giardia lamblia* and *Trichomonas hominis*. No treatment was given to these patients.

SUMMARY

The records of 105 patients studied on the gastrointestinal ward of a general hospital are analyzed. Attention is drawn to the latent and chronic nature of the diarrheal diseases acquired while the patient was serving outside the United States.

Carriers of *Entamoeba histolytica* should be treated to prevent the subsequent development of dysentery. The importance of sigmoidoscopic examination and the collection of purged stools in the diagnosis of amebiasis is emphasized. The need for early clinical diagnosis in amebic hepatitis and for prompt

TABLE 10 Data in 6 Cases of Sprue Contracted in the Pacific Theater (Continued)

Weight Loss	TOTAL STOOL FAT	MAXIMUM FREE GASTRIC ACID	SERUM ALBUMIN	SERUM GLOBULIN	RED CELL COUNT	HEMOGLOBIN	GLUCOSE TOLERANCE TEST (MAXIMUM)	RESPONSE TO STRICT LOW-FAT DIETARY
lb	gm	units	gm/100 cc	gm/100 cc	$\times 10^5$	gm/100 cc	mg/100 cc	
62	73.6	15	4.4	1.2	4.1	12.1	95	Excellent
45	18.1	—	5.4	1.0	5.6	10.5	132	Good
53	46.8	12	5.4	1.0	4.7	13.9	108	Excellent
57	36.1	55	5.4	2.3	4.9	13.0	103	Good
13	31.2	44	—	—	4.5	12.9	150	Good
29	15.7	40	5.1	1.1	4.9	14.3	137	Good
69	11.9	49	—	—	3.2	10.8	95	Excellent

it negative in the United States. In 4 cases a clinical diagnosis of schistosomiasis had been made overseas, but since ova were not found overseas or in the United States the diagnosis is not certain. It is interesting to note that no carriers or mild cases of schistosomiasis were found in patients admitted to the hospital with a diagnosis other than schistosomiasis. All the patients with schistosomiasis were transferred to a special ward for treatment and follow-up study after the amebiasis had been brought under control. Five of the men in this group were found to have schistosomiasis and were treated overseas; they were stool negative on arrival in the United States. Five other patients treated in the United States for the first time were also cured after one or two courses of methylresorcinol.

treatment with emetine, as well as with further medication with carbarsone or one of the iodine containing oxyquinolines, is stressed. Tissue invasion, usually evidenced by a positive complement-fixation test, may produce stricture of the rectum and appendicitis, as well as granulomatous lesions. Patients with amebic dysentery who show any evidence of rectal involvement — either by proctoscopic examination or from the presence of blood in the stools — should be treated with retention enemas. Contrary to current belief, vioform suspension is nonirritating and most convenient for retention enemas in the treatment of amebic dysentery. It is advisable to give an oral course of this drug in conjunction with retention enemas, thus obviating the use of chiniofon and carbarsone, which are likely to aggravate diarrhea.

Ulcerative colitis apparently develops after severe amebic dysentery as well as after bacillary dysentery. Men who have served overseas, especially those who have had amebic dysentery, are subject to re-

the loss of a great deal of weight there may be signs of vitamin deficiency. These patients, well to a diet strictly limited in fat and high in protein and carbohydrate.

TABLE 11 *Results of Hookworm Treatment*

NO OF TREATMENTS	OVERSEAS		NO OF TREATMENTS	IN THE UNITED STATES		NOT FOLLOWED
	POSITIVE STOOL EXAMINATION IN UNITED STATES	NEGATIVE STOOL EXAMINATION IN UNITED STATES		POSITIVE STOOL EXAMINATION	NEGATIVE STOOL EXAMINATION	
1	7	8	1	3	5	3
2	3	3	2	4	2	2
3	1	0	3	1	0	0
4	1	1	4	1	0	0
5	0	0	Variable*	5	3	2
6	1	0				
7	2	0				
8	1	0				
9	0	0				
10	0	1				
Totals	16 (55%)	13 (45%)		14 (45%)	10 (32%)	7 (23%)

*Increased dose of tetrachlorethylene, as well as oil of chenopodium

current attacks of diarrhea. This condition responds gradually to rest and diet and is sometimes helped by antiamoebic treatment.

A large proportion of cases considered as unclassified dysentery will be found to have steatorrhea.

Hookworm infestation is frequent in troops in the Pacific area. Symptoms from this infestation are rare, and although treatment with tetrachlorethylene may not eradicate all the parasites it is not necessary to continue treatment after two courses of the drug.

TABLE 12 *Data in 16 Cases of Strongyloidiasis*

THEATER	DATA OVERSEAS								DATA IN UNITED STATES									
	SYMPTOMS	POSITIVE STOOLS	WHITE-CELL COUNT		GENTIAN VIOLET		ROUTE EMPLOYED	SYMPTOMS	POSITIVE STOOLS	WHITE CELL COUNT		EOSINOPHILS	CHIEF CLINICAL DIAGNOSIS	GENTIAN VIOLET		ROUTE	POSITIVE STUOL EXAMINATION	
			x ²	%	mg/day	Period				x ³	%			mg/day	Period			
Pacific	Yes	Yes	7	26	125	4	Intravenous	Yes	Yes	8	2	Strongyloidiasis	180	10	Oral	Yes		
					250	3	Intra-duodenal					Strongyloidiasis	300	5	Oral	Yes		
												Strongyloidiasis	180	30	Oral	Yes		
European	Yes	Yes	9	9	—	—	—	Yes	Yes	14	4	Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	Yes	11	60	—	—	—	Yes	Yes	11	29	Strongyloidiasis	300	5	Oral	No		
												Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	No	32	69	—	—	—	Yes	Yes	10	7	Strongyloidiasis	180	10	Oral	No		
Pacific	No	—	—	—	—	—	—	No	Yes	10	12	Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	No	30	62	—	—	—	Yes	Yes	8	1	Strongyloidiasis	180	10	Oral	Yes		
Pacific	No	—	—	—	—	—	—	Yes	Yes	14	3	Strongyloidiasis	300	5	Oral	Yes		
												Strongyloidiasis	180	30	Oral	Yes		
Pacific	Yes	Yes	8	24	125	3	Intravenous	Yes	Yes	7	21	Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	Yes	7	20	—	—	—	Yes	Yes	10	28	Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	Yes	10	21	250	4	Intra-duodenal	Yes	No	7	4	Steatorrhea	—	—	—	—		
								No	Yes	9	12	Strongyloidiasis	180	10	Oral	No		
Pacific	No	Yes	—	—	—	—	—	Yes	Yes	9	12	Strongyloidiasis	180	10	Oral	No		
Pacific	Yes	Yes	8	36	180	30	Oral	No	Yes	13	32	Strongyloidiasis	180	10	Oral	No		
China and India-Burma	No	—	—	—	—	—	—	No	Yes	12	5	Strongyloidiasis	180	10	Oral	No		
China and India-Burma	No	—	—	—	—	—	—	No	Yes	12	5	Strongyloidiasis	180	10	Oral	No		
European	Yes	Yes	8	4	250	1	Intra-duodenal	Yes	Yes	8	6	Strongyloidiasis	180	10	Oral	No		
					180	30	Oral											
Pacific	No	Yes	19	60	180	12	Oral	No	Yes	9	35	Strongyloidiasis	180	10	Oral	No		
					160	1	Intra-duodenal											

on analysis of the twenty-four-hour stool for fat. Stool analysis can be simply accomplished by wet extraction. Most cases of steatorrhea correspond to early stages in the development of sprue, and despite

have been given. Strongyloidiasis when it occurs may cause marked eosinophilia suggesting schistosomiasis. Treatment with gentian violet is not always effective, and the need for further study is suggested.

illary dysentery and other intestinal parasitoses, with the exception of schistosomiasis, did not present any special problems in diagnosis or treatment.

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SURGICAL TREATMENT OF ASCITES

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ASCITES is a problem frequently encountered and often unsatisfactorily treated. An adjunct to the therapy of ascites has been tried in a limited number of cases and has seemed sufficiently helpful to warrant reporting.

Attempts to obtain more lasting relief from ascites have been many and varied. In 1896 Drummond and Morison¹ reported the first surgical treatment of ascites. Talma,² in 1898, is usually credited with the original suggestion for the surgical relief of ascites, and the operation — omentopexy — has come to be known as the Talma-Morison operation. Morison's patient lived two years after the operation. Monprofit³ reported 224 cases treated by the Talma-Morison operation up to 1904. Thirty-one per cent of this group were successfully relieved of their ascites for varying periods. Noetzel,⁴ in 1919, and Mayo,⁵ in 1924, reported smaller groups in which the operative mortality was high and good results relatively few. Hughson⁶ considered the operation to be without value. Grinnell⁷ obtained relief from ascites in only 2 of 23 patients operated on. In 1943 Cates⁸ reviewed the patients treated by omentopexy at the Los Angeles County Hospital during the previous five years. Thirty-eight patients who were operated on were compared with 172 treated medically; follow-up study led to the conclusion that the surgical intervention did not improve the prognosis. Operative mortality was high. 42 per cent of the patients died within two weeks of the operation, presumably because of under-nutrition, the susceptibility of patients with cirrhosis of the liver to shock and tympanites, poor wound healing associated with hypoproteinemia, and

the greater danger of administering anesthesia because of failure of the cirrhotic liver to detoxify the anesthetic agent.

The operation itself is a simple one. An epigastric incision is made just to the right of the midline through the abdominal wall, the peritoneal cavity is opened, and a portion of the omentum is withdrawn. A second lower incision is made through the skin and muscle down to the posterior aponeurosis and peritoneum. The rectus muscle is separated from its posterior attachment, and the omentum is drawn from the upper incision down into the extraperitoneal pocket thus formed. The rationale is simply to establish a portal collateral circulation via the omentum and the vessels of the abdominal wall. All the earlier attempts at surgical control of ascites were somewhat impeded by failure to take into consideration and to treat adequately other contributory factors, such as hypoproteinemia and poor liver function. Evaluation of omentopexy over a long period, however, seems to indicate that it leaves much to be desired.

Another attempt at the surgical treatment of ascites is described by Ferguson,⁹ who reports a case in which a right nephrectomy was performed and the renal pelvis anastomosed to the peritoneum along the peritoneal gutter beside the ascending colon. Since omentum blocked the outlet in this position, the site of anastomosis later had to be shifted to the lower part of the right rectus muscle. This, of course, simply provided an outlet for the ascitic fluid via the bladder and thus obviated repeated paracenteses. The protein content of the fluid, however, was still lost to the patient.

A third method, aimed at relieving the portal hypertension of cirrhosis, is described by Blakemore and Lord¹⁰ and by Whipple¹¹. In 5 cases the blood was shunted from the portal to the caval system by removal of the spleen and left kidney and by

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anastomosis of the splenic and left renal veins by means of an endothelial-lined vitallium tube. In 5 other cases portacaval shunts (Eck fistulas) were produced by end-to-side anastomoses of the portal vein to the inferior vena cava over vitallium tubes and ligation of the portal vein between operations. Whipple stated that all 10 patients survived the operation but that a follow-up period of three years or more would be required to determine the value of these portacaval shortcircuiting procedures.

The method of treating ascites described below is by the insertion of a glass button into the abdominal wall. The origin of this therapeutic device is obscure. It was first encountered by one of us (RCC) in New Orleans, where it was used by Dr. Julian Rickles,¹² who, in turn, had heard about it from Dr. Douglas Donath,¹³ who had been using it at the Marine Hospital in New Orleans. Communication with Dr. Donath revealed that he, too,

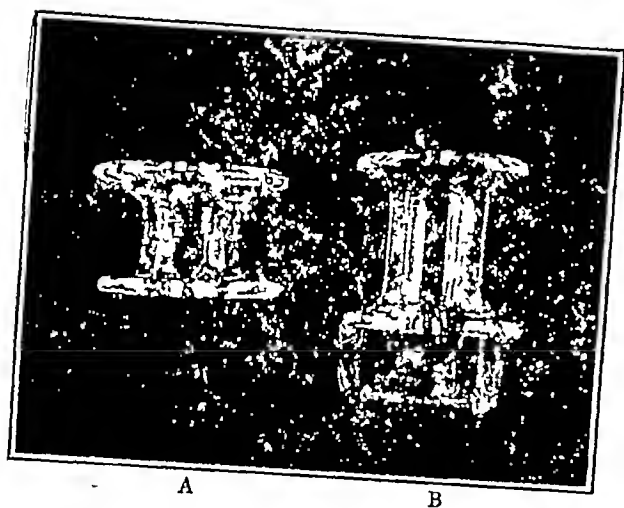


FIGURE 1 Abdominal Buttons

A — the button used by former workers. B — the button with an added glass plate to prevent omental impaction in the core.

had tried to ascertain the origin of the glass button and had traced it as far as a British Army surgeon in Egypt but had been unable to learn the name of its originator. One reference to the use of a similar device was found in the literature. Tannahill,¹⁴ in 1930, reported a single case of cirrhosis of the liver with ascites treated by the insertion of two glass buttons — one under the sheath of the upper rectus muscle and the other lateral to it in the upper quadrant. These were smaller buttons than those used by us, and Tannahill called them "Paterson buttons." He attributed the idea to Professor Peter Paterson, of Glasgow University. His patient required one postoperative paracentesis but subsequently did well.

Lichtman¹⁵ states that in 1922 Boccardo used a glass tube resembling a collar button to drain

ascitic fluid into the subcutaneous tissues. reference was not found in the literature.

The button as used by previous workers is in Fig 1A. We have added the top plate, as in Fig 1B. The button can be made by any petent glass blower. The flanges are approximately 2.0 cm in diameter, and the bore is 0.6 cm. The button itself varies from 1.0 to 1.5 cm in length and the added glass plate lies approximately 0.6 cm below the lower flange.

This button is inserted into the anterior rectus sheath, the lower flange, with the glass plate, lying just inside the peritoneum. The rectus sheath fat between the flanges, and the distance between the flanges can be varied to accommodate various thicknesses of the sheath in different patients. The anterior rectus sheath is sutured tight under the upper flange, and the skin closed. The function of the button is simple: it merely allows ascitic fluid to pass through its core and thus into the subcutaneous tissues, where it is absorbed as edema fluid. We have added the top plate in an attempt to prevent the omentum from blocking the outflow of ascitic fluid by becoming impacted in the core of the spool as happened in some cases in which it was used in New Orleans.¹²

One great advantage of this therapeutic device is its ease of application. It is known that patients with hepatic cirrhosis do not tolerate major surgery well. Malnutrition, susceptibility to shock and tympanites contribute greatly to the high operative mortality. Secondly, wound healing is poor unless vitamin C and a great deal of protein, preferably as intravenous plasma or amino acids, are given. Finally, the anesthetic tolerance is poor, since the damaged liver detoxifies the anesthetic agent poorly, yet large amounts of anesthetic are usually required for satisfactory anesthesia in patients with alcoholic liver cirrhosis. For these reasons major surgical procedures such as those outlined above are at best limited in their applicability.

The insertion of the button is a simple procedure and may be done under local anesthesia if desired, although spinal anesthesia was used in all our cases. The site selected may be over either the right or the left rectus muscle below the level of the umbilicus. A 6 cm midrectus incision is made and deepened through the muscle layer to the peritoneum, which is nicked to allow the insertion of a suction tube to remove the ascitic fluid. The opening in the peritoneum is then made the same length as the skin incision. The peritoneum and anterior rectus fascia at the lower margin of the wound are grasped with an Ochsner clamp, and the fat layer below the lower end of the wound freed up over an area from 8 to 10 cm below the lower margin of the wound. After retraction of the skin and fat layer at the lower part of the wound downward and pulling upward on the Ochsner clamp

holding the peritoneum and anterior rectus fascia, a stab wound is made about $\frac{1}{4}$ cm below the lower margin of the wound going through the anterior rectus fascia, muscle and peritoneum. The stab wound is enlarged enough to allow for the insertion of the button. A silk purse-string stitch is then taken in the peritoneum around the button to fix it in place, a similar stitch is taken in the anterior rectus fascia after the rectus muscle has been placed between the flanges of the button. The main wound is then closed in layers without drainage.

Ideally, of course, sufficiently good treatment of the underlying disease so that ascites disappears spontaneously is the goal of therapy. Unfortunately, such a result is not always or even often possible, diuretics and repeated paracenteses are the rule. The mechanism of the production of ascites in cirrhosis is not entirely clear. It has been suggested that ascites is the result of hypoproteinemia, although the relation between ascites and the serum protein or albumin level is not always a parallel one. It has also been suggested that ascites is the direct result of portal hypertension — a hypothesis difficult to prove or disprove. The theory of Ralli et al.¹⁸ that the ascites is due to an antidiuretic hormone — possibly to failure of the diseased liver to destroy posterior pituitary antidiuretic hormone — is an interesting concept that fails, however, to explain the absence of edema in many patients with definite ascites.

The avoidance of repeated paracenteses is the purpose of the abdominal button, which is a purely symptomatic measure but has another advantage: it returns to the patient his own ascitic fluid together with its protein content. The protein loss from repeated paracenteses is not inconsiderable. In some clinics it is the practice to reinject the ascitic fluid intravenously so that the protein content will not be lost to the patient. The abdominal button does this automatically, the ascitic fluid draining through the core of the button becomes edema fluid as fast as it is formed and is absorbed as such. Thus the button may be regarded as a mechanism by which the patient with ascites is given a constant slow clysis of his own ascitic fluid so long as such fluid is formed.

This procedure was employed in 7 cases. One recent case is not included in this report. The following case report is typical.

CASE 2 W. D. (P. D. H. 14-421), a 48-year-old food broker entered the hospital on April 23, 1945. The alcoholic intake had averaged a quart of Bourbon whiskey daily for many years. During the previous year food intake had been confined to a small evening meal daily. In May, 1942, a Civil Service physical examination had been negative. Except for a bleeding hemorrhoid in October, 1942, the patient remained well until the winter of 1944-1945, when he began to feel weak and tired. He lost 20 pounds in weight during the winter, and 5 weeks before admission he developed an upper respiratory infection, with general malaise followed a week later by jaundice. At that time he completely lost his appetite, the food intake being confined to fruit juices. Alcohol was not used. Self-administered "salts" for several days produced diarrhea and rectal bleeding. Bowel

movements were otherwise light in color, the urine was dark and there was progressive swelling of the abdomen. Four days before admission abdominal paracentesis yielded 6 liters of fluid. Following this there were dysphagia and nausea, and a small amount of blood was vomited.

Examination revealed an obese, deeply jaundiced and rather acutely ill and confused man. The heart and lungs were essentially normal. The abdomen was tense and protuberant, extending well above the costal margin. There were shifting dullness and a fluid wave. The liver was palpated $\frac{1}{4}$ fingerbreadths below the right costal margin. The spleen was not felt. No edema was noted. Spider telangiectases were present.

Examination of the urine showed a + test for albumin, a ++++ test for bile and approximately 1 white cell and 1 red cell per high-power field. Examination of the blood showed a red-cell count of 3,340,000, with a hemoglobin of 64 per cent, and a white-cell count of 20,500, with 90 per cent neutrophils, 31 per cent of which were band cells. The serum bilirubin was 28 mg per 100 cc, 21 per cent of which was direct, the nonprotein nitrogen was 36 mg, the total protein 5.9 gm, the albumin 2.9 gm and the globulin 3.0 gm per 100 cc. The blood Hinton test was negative. The sedimentation rate was 29 mm in 1 hour. The stools gave ++++ benzidine and guaiac reactions. The bromsulfalein test showed 98 and 82 per cent retention of the dye at 30 and 60 minutes respectively. A cephalin-flocculation test was +++ in 24 hours. Two weeks later the total protein was 5.5 gm, the albumin 1.7 gm and the globulin 3.8 gm per 100 cc, and the bromsulfalein test showed 67 and 48 per cent retention of the dye at 30 and 60 minutes respectively. The cephalin-flocculation test was ++ in 24 hours. The serum bilirubin was 24.8 mg per 100 cc indirect and 19.8 mg direct. The prothrombin time was 50 per cent normal throughout.

The patient was given a high-protein, high-carbohydrate, low-fat, low-salt diet, with 576 gm of powdered yeast three times daily and supplementary thiamine chloride and vitamin B complex by injection. Crude liver extract and vitamin K were also given by injection. Ammonium chloride and Mercupurin provided a fair diuresis. Abdominal paracentesis was discontinued after 900 cc of fluid had been removed, but drainage continued for several days, a total of 8 pounds in weight being lost during the hospital stay. The patient was discharged only slightly improved and advised to remain on diet and vitamin therapy.

Following discharge the hepatitis improved slowly but steadily. The color of the stools became normal, the urine became lighter, and the patient felt somewhat improved. Repeated abdominal paracenteses were required, however, to control the ascites, and for this reason on July 13, after the jaundice and hepatitis had almost disappeared, an abdominal button was inserted under spinal anesthesia. The postoperative course was uneventful. On getting up the patient developed marked edema of the thighs, scrotum and penis, despite the fact that all the ascitic fluid had been aspirated at the time of operation. This edema was gradually absorbed, however, but when the patient was last heard from slight edema was noticed (evidence that ascitic fluid was still forming but was draining via the button). Shortly after the operation he reported that he felt better than he had in years. Six months postoperatively he was completely symptom free, except for minimal edema of the lower abdominal wall, had resumed full activities and had regained his normal weight and strength.

A summary of the data and results in all 6 cases is presented in Table 1. As can be seen the 5 cases were fairly typical of Laennec's cirrhosis in various stages of compensation. Four patients had been confirmed alcoholic addicts for many years. The patient in Case 5 denied the use of alcohol, and the dietary history as given was adequate, yet the clinical picture left little doubt of the diagnosis. All patients showed typical spider telangiectases, and all had low serum proteins, with reversal of the albumin-globulin ratio. The prothrombin time was significantly prolonged in all except Case 4, and bromsulfalein retention was marked in all.

TABLE 1 Data and Results in 6 Cases in Which the Abdominal Button Was Inserted

CASE No.	AGE	SEX	AMOUNT OF ALCOHOL TAKEN DAILY	DURATION OF ALCOHOLISM	DURATION OF ASCITES	DEGREE OF ASCITES	SERUM BILIRUBIN mg./100 cc.	TOTAL PROTEIN gm./100 cc.	SERUM ALBUMIN gm./100 cc.	SERUM GLOBULIN gm./100 cc.	PROTHROMBIN TIME sec.	BRONSULALEIN RETENTION* 30 min % of dye	BRONSULALEIN RETENTION* 60 min % of dye	RESULT OF TREATMENT
1	32	M	3 quarts of whisky	15 yr	7 mo	++++	1.5	6.0	1.7	4.3	46 (control, 23)	89	88	Patient symptom free and taking part in full activities 11 mo after operation
								6.2	3.1	3.1		35	16	
								7.7	4.5	3.2		20	9	
								7.3†	5.0†	3.3†	Normal†	11†	4†	
2	48	M	1 quart of whisky	Many	1	++++	28.0	5.9	2.9	3.1	40 (control, 20)	98	82	Patient symptom free and taking part in full activities 7 mo after operation, slight edema of thigh
								5.5	1.7	3.9		67	48	
3	44	M	2 quarts of whisky	Many	3½	++++	14.8	6.9	1.9	5.0	40 (control, 24)	—	—	Death 6 days after operation from peritonitis, gastro-intestinal hemorrhage and advanced cirrhosis
4	38	M	15-20 bottles of beer	15-20	8	++++	—	5.2	1.8	3.4	21 (control, 20)	—	53	Patient symptom free, except for slight edema, and taking part in full activities 5 mo after operation
								5.4	2.9	2.5	23 (control, 24)			
5	48	F	None	—	5	++++	2.9	6.0	1.3	4.7	26 (control, 22)	40	23	Patient convalescing and symptom free, taking part in restricted activity
6†	68	F	—	—	—	—	—	—	—	—	—	—	—	Poor healing of wound initially, patient doing well, except for troublesome edema 2 mo after operation

*Two milligrams of bronsulalen per kilogram of body weight injected intravenously

†After operation

‡This patient had chronic constrictive pericarditis

except Case 3, in which the test was not done because of the obviously severe hepatic insufficiency

The results may be considered good in all cases except Case 3, in which the operation was performed, despite a severe hepatic insufficiency, because of constant rapid accumulation of ascitic fluid. This patient was confused and deeply jaundiced, and showed the fetor hepaticus of cholemia throughout the hospital course. Autopsy revealed peritonitis and a stomach and upper bowel full of blood from a ruptured esophageal varix, in addition to advanced cirrhosis. A fatal outcome could have been predicted even without the button insertion and the peritonitis, which was obviously directly attributable to the button.

Other therapy that these patients received, of course, cannot be disregarded. This consisted of a high-protein, high-carbohydrate, low-fat diet, as well as 50 gm of brewer's yeast daily, 3 gm of choline chloride a day and, in most cases, vitamins A, B and D. Diuretics were given and preoperative abdominal paracenteses were performed as needed. The patient in Case 1 also received large amounts of plasma before operation.

Because it might be argued that these patients were cured of ascites by nonspecific measures — in other words, by the intensive medical therapy directed toward the underlying disease — Case 6 is of particular interest. This patient had chronic constrictive pericarditis. She was first admitted to the Joseph H Pratt Diagnostic Hospital in 1940, when the diagnosis was established. Pericardiectomy was contraindicated because of severe underlying myocardial damage. Ascitic fluid, which had continuously accumulated for over six years, required repeated paracenteses, despite fluid and sodium restriction as well as the use of diuretics. The therapeutic regimen was altered only in that a button was inserted, despite the fact that a mechanically impaired heart and a high venous pressure rendered mobilization of the consequent edema difficult if not impossible. Since paracenteses were becoming necessary in increasing frequency and the potential absorptive surface is greater for edema than for ascites a trial of the button seemed warranted in this case. On a continued regimen of restricted salt and fluid the patient remained relatively free of symptoms after the insertion of the button. The edema of the lower abdominal wall and thighs continued to be troublesome. As anticipated the edema fluid was mobilized with difficulty, and mercurial diuretics were therefore frequently required. The patient was able to carry on restricted activities, however, and felt well. Adequate function of the button may be assumed from the absence of ascites, as well as the constant accumulation of edema.

It is too early to arrive at any final evaluation of the results. Bearing in mind that the only purpose of the abdominal button is the relief of ascites, it may be said that in this respect it is successful.

Adequate function of the button was assured in Cases 2, 4, 5 and 6 by continuous slight edema of the lower abdominal wall and thighs, as well as by the absence of ascites. It is possible that in Case 1 ascitic fluid simply stopped forming as a result of medical therapy. Other users of a button have occasionally found that the omentum became impacted in the core and thus prevented adequate functioning of the button. This complication did not occur in any of the present series, possibly owing to the addition of the top plate. The one patient (Case 1) who was readmitted for follow-up studies showed clinical recovery. Patek's¹⁷ criteria for clinical recovery are weight gain and strength for full activity, disappearance of ascites, edema and jaundice, and return to normal of laboratory findings. Preliminary reports indicate that all the cases of cirrhosis, except Case 3, fulfill such criteria. The patient in Case 6, of course, benefited only in that the ascites was converted to edema, which is perhaps more easily dealt with.

SUMMARY

The literature concerning previous attempts at surgical treatment of ascites is reviewed. A method for the treatment of ascites is presented. This consists of a glass button inserted into the lower rectus sheath so that ascitic fluid may drain from the peritoneal cavity into the subcutaneous tissues and be absorbed as edema fluid.

Five cases of Laennec's cirrhosis of the liver and 1 of chronic constrictive pericarditis are presented, in all of which the ascites was treated by the insertion of the button. The rationale for the use of the button is purely to obviate repeated abdominal paracenteses. Its main advantage over previous surgical measures for the relief of ascites is its simplicity of application. An additional value is that it returns to the patient his own ascitic fluid together with its protein content as a constant slow clysis so long as the fluid is formed.

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TUBERCULOSIS OF THE GENITOURINARY TRACT AMONG SOLDIERS IN WORLD WAR II*

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IN World War II, in the United States Army, all patients with tuberculosis — whether pulmonary or otherwise — were sent either to Fitzsimons General Hospital, Denver, Colorado, or to Bruns General Hospital, Santa Fe, New Mexico. Of the two hospitals the former was considered the senior and more important, since it was older and larger and was a permanent installation. The treatment of tuberculous patients at Fitzsimons General Hospital was typical of that in the majority of cases in the Army, and as chief of the Section of Urology from January to December, 1945, I had the opportunity to observe and treat a good deal of the tuberculosis of the genitourinary tract that occurred in the Army during that period.

The incidence of pulmonary tuberculosis was 0.9 per 1000 soldiers per year before the taking of chest x-ray films prior to separation, but increased to 1.2 per 1000 after these films had been taken. On the basis of the patient population at this hospital, the ratio of occurrence of pulmonary to genitourinary tuberculosis was approximately 33:1 — a yearly incidence of genitourinary tuberculosis of about 0.03 per 1000 soldiers.

Many different races were represented, including the White, Jewish, Negro, American Indian, Mexican, Filipino, Chinese and Eskimo. Seventeen per cent of the patients were Negroes, and there were an appreciable number of American Indians. In view of the higher percentages of these races among the tuberculosis patients than in the Army as a whole, it seems fair to conclude that they are more susceptible than the average soldiers. More than a third of the patients (38 per cent) were from the Army Air Forces, including some flying and some ground personnel. More than half the patients had been overseas, usually for a good many months, in various areas, England, Europe, the Mediterranean, the Pacific, India and Alaska, — and there was no obvious predominance of patients with tuberculosis from any one theater. Most of the patients were not in the youngest Army age group but were a little older, the average age being twenty-eight and a half years. Practically none of them gave a history suggestive of previous tuberculosis, which of course is natural in view of the fact that men with a known history of tuberculosis are not taken into the Army. Also, surprisingly few patients gave a history of tuberculosis in the immediate family or of known exposure to it.

The tuberculosis of the genitourinary tract seen in the soldiers consisted almost entirely of either

renal tuberculosis or tuberculosis of the epididymis, the latter being observed in a ratio of 4:3. Both renal and epididymal tuberculosis, however, frequently occurred in the same soldier, 40 per cent of the renal cases also had tuberculosis of the epididymis, and 30 per cent of the epididymal cases had concomitant renal tuberculosis. The fact that unexpectedly few patients — only about 20 per cent of the total — had demonstrable evidence of either active or inactive pulmonary tuberculosis was quite surprising if one believes in Louis's law "tuberculosis of any part is attended by tuberculosis of the lungs," and that the original focus for tuberculosis of the genitourinary tract is in the lungs. When pulmonary tuberculosis was found, it was more frequently associated with renal tuberculosis than with epididymal tuberculosis, since it occurred in more than a quarter (28 per cent) of the cases of renal tuberculosis and in 1 in 8 (13 per cent) of epididymal tuberculosis. Extrapulmonary manifestations of active tuberculosis did not usually coexist with genitourinary tuberculosis, but when such an association did occur the most frequent concomitant was bone and joint tuberculosis. Also found occasionally were psoas abscess, tuberculosis of cervical lymph nodes, ophthalmic tuberculosis and tuberculosis of the skin.

In almost all patients the renal tuberculosis was discovered in an early stage, — before it had become advanced, — and the lesions characteristic of advanced renal tuberculosis, such as extensive destruction of the kidney, dilated thickened and tortuous ureters, and severe inflammation and ulceration of the bladder, were not observed.

The first symptoms of renal tuberculosis were as a rule mild and occasionally entirely absent, the disease being detected only as a result of a search for the cause of a persistent pyuria. Symptoms usually consisted of mild discomfort in the back — sometimes accompanied by fever — or of somewhat increased urinary frequency. There were few cases in which bladder symptoms were prominent, and cystoscopy rarely showed the bladder to be involved to any appreciable degree. Microscopic pathological examination, however, showed the ureter to be involved to some extent in many of the cases of renal tuberculosis, except the extremely early ones.

In an appreciable number of cases the pyelogram gave evidence that was inconclusive and was suggestive of only cicatricial changes, and in a few cases the pyelograms, both intravenous and retrograde, were not abnormal and gave no help. It was found that retrograde pyelograms gave a better and more

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endable filling and delineation of the kidney than a venous urogram. On various occasions, when intravenous urograms gave a picture that was either inconclusive or only faintly suggestive, the retrograde pyelogram delineated the kidney much more clearly and completely and sometimes indicated an unsuspected lesion, such as a cavity communicating with a calyx. Therefore, in any case in which the intravenous pyelogram was not quite satisfactory, clear or conclusive, retrograde pyelograms were done. In cases in which both intravenous and retrograde pyelograms were inconclusive it was necessary to depend largely on cultures of the urine, which were found to be absolutely reliable.* In no case did a kidney that had given a positive culture for tuberculosis fail to show the disease on pathological examination after removal, even though the pyelogram had appeared normal. The routine was to culture ureteral specimens of urine from each kidney and also four twenty-four-hour specimens of bladder urine, which were taken simply as a check on the kidney cultures. No case with a positive kidney culture gave negative cultures on the twenty-four-hour urine specimens, if such an event had occurred all cultures would have been repeated. If the results of the cultures did not seem in accordance with the pyelograms, or if there was a question whether or not the supposedly normal kidney was infected, the cultures were repeated before any operation, and in no case was nephrectomy performed until the healthy kidney had been shown to give a negative culture. In comparing the cultures with the stained smears of the urine, it was found that the former were much more accurate. In most cases in which the kidney urine gave a positive culture, which was later corroborated by the finding of tuberculosis in the removed kidney, the stained smears from that kidney were reported negative for tubercle bacilli. Many more positive smears were found in concentrated twenty-four-hour specimens of urine than in kidney specimens obtained at cystoscopy from the same patient, presumably owing to the greater total number of tubercle bacilli. Of course, it is true that the persistence of the person who examines the stained smear and the time at his disposal to examine the slide naturally make a great difference regarding whether or not acid-fast bacilli are found, but the cultures were nevertheless more accurate and sensitive than the smears in detecting tubercle bacilli. When the smears were positive, the cultures were almost always also positive. In a few twenty-four-hour urine specimens with positive smears, however, the cultures were negative, but after repeated smears and cultures the conclusion was reached that the acid-fast bacilli seen on the slide were contaminants, probably smegma bacilli that were indistinguishable on stain. This was another fact suggesting that the culture

was more accurate and reliable than the smear. No guinea-pig inoculations were used at Fitzsimons General Hospital, although they were often used at other Army hospitals and seemed to produce reliable results. Cultures are quite reliable and have the advantage over guinea-pig inoculations in that they are less expensive and much less space is occupied.

Since cultures took two months for completion and occasionally had to be repeated, many patients spent a considerable time in the hospital before operation, but definite knowledge of the status of both kidneys was regarded as absolutely imperative before operation. Also, in view of the facts that tuberculosis is a constitutional disease and that the lesions in the genitourinary tract are secondary to tuberculosis elsewhere in the body, a careful search was made for other foci of infection. Furthermore, in agreement with other workers in this field, it was believed that a sufficiently long, unhurried period of rest and hospitalization both before and after operation improved the patient's general condition and resistance to tuberculosis, so that the results in general were improved, the patients tolerated surgery better, wound healing was better with less tendency to formation of chronic draining sinuses, and surgery was less apt to spread the disease. Unless the disease in the kidney or elsewhere, such as in the lungs, was active enough to make bed rest mandatory, the soldiers were usually not kept on strict bed rest but were allowed to be up some of the time and to partake in restricted activity.

In common with the vast majority of those who have had the opportunity to observe renal tuberculosis, it was believed that the normal kidney does not filter tubercle bacilli from the blood stream to the urine, that tubercle bacilli in the kidney urine obtained by ureteral catheterization denote renal tuberculosis, and that any renal lesion that has progressed so far as any degree of ulceration will not heal spontaneously but will tend to progress despite sanatorium care. Therefore, when the diagnosis of tuberculosis of one kidney had been made and the other kidney was free of disease, nephrectomy was carried out, unless it was contradicted by some complication in the patient's condition. Bilateral renal tuberculosis was exceedingly rare, and was always found in association with active tuberculosis elsewhere in the body. Nephrectomy was not performed in any case of bilateral tuberculosis. If a case of bilateral disease is encountered, however, in which one kidney is badly diseased and destroyed and the other has only a minimal trace of the disease, it is my opinion that nephrectomy of the badly damaged kidney may be advisable. In such a case it is well known that nothing can stop the badly damaged kidney from continuing to deteriorate, and its removal may ameliorate or prevent the development of an excruciatingly painful tuberculous

*The culture medium used was Pettragnani's medium, whose chief constituents are potatoes, milk and eggs.

cystitis and also removes a tuberculous focus from the body. If active pulmonary tuberculosis existed, nephrectomy was not done until the process in the lung was arrested or quiescent to a point where operation was no longer contraindicated. In fact, in such cases, operation was considered desirable to remove a tuberculous focus from the body.

The type of operation done was the ordinary lumbar nephrectomy. The healing was so satisfactory in practically all cases that there seemed to be no object in doing a nephroureterectomy, especially since this procedure would have entailed another incision and put the patient through a more serious operation, increasing the likelihood of morbidity and mortality. In most cases the ureter was simply ligated, carbolized and dropped back into the wound. In some cases in which the ureter was dilated, thickened, tortuous and obviously diseased, it seemed better insurance against chronic sinus formation in the nephrectomy wound to bring the upper end of the remaining ureter out through a tiny stab wound below the main wound. In these soldiers as a group, however, the renal tuberculosis was discovered in an early stage and there were comparatively few of the dilated, thickened and tortuous ureters seen in advanced renal tuberculosis. The wounds were drained with soft rubber drains for twenty-four to forty-eight hours to let out serum, after which the drains were removed, because it was believed that leaving them in might help create a chronic sinus. Most of the nephrectomies were done under spinal anesthesia, which had the advantage that the patients could start taking frequent deep-breathing exercises immediately after operation as a prophylaxis against such pulmonary complications as atelectasis. For the same reason, the patients were made to lie with the operated side down for much of the time for the first twenty-four hours. If the spinal anesthesia wore off during the operation, it was supplemented with a small amount of Pentothal Sodium intravenously. To avoid thrombophlebitis, the patients were allowed out of bed beginning the day after operation, in fact, they occasionally stood up beside the bed on the evening of the operation, to try to void in a more natural position. Despite the fact that the patients continued to get out of bed every day beginning the day after operation, no weak or bulging scars resulted. No wounds broke down, although in 1 case much of the skin incision broke open. There were several cases in which a small draining sinus persisted for weeks. Almost to a man the patients withstood nephrectomy well, and there were no postoperative deaths in the twelve months ending in December, 1945.

Tuberculosis of the epididymis was the most frequent form of genitourinary tuberculosis encountered — 68 per cent of the total. This condition was bilateral in slightly more than a quarter (28 per cent) of the cases and unilateral in the rest. In the cases of epididymal tuberculosis renal tuberculosis was

also present in 30 per cent and pulmonary tuberculosis in 13 per cent.

The first symptom of epididymal tubercle noticed by the soldiers was usually a somewhat full swelling in the affected scrotum that came gradually over a period of weeks or months. Sometimes pain was absent, whereas the pain and swelling occasionally developed rapidly in the course of a few weeks or even a few days. Most soldiers noticed this condition themselves, but in rare cases it was discovered during a routine general physical examination. The diagnosis was made largely on the basis of the physical examination, which characteristically revealed the whole epididymis to be grossly enlarged, hard, nodular and irregular, but not extremely tender. When only the lower pole of the epididymis was grossly diseased there was a typical hard mass at the lower pole in the shape of a large, thick, irregular button. This was practically always adherent to the skin of the scrotum, which was by far the most frequent site for a draining sinus. In a few cases the tuberculous process had definitely spread from the epididymis to involve the testis. The vas deferens was involved in most cases, and was frequently thickened and occasionally beaded. The spermatic vesicle on the diseased side and also the prostate often had indurated, irregular and nodular areas, evidence that they were also involved in the pathological process. In more than a third of the cases (37 per cent) a draining sinus had become established before hospitalization, usually after spontaneous rupture of a scrotal abscess but occasionally following surgical drainage of an abscess. In all cases in which sinuses had once become established spontaneous healing did not take place, and although the sinuses sometimes healed temporarily, they continued to drain until the diseased epididymis — as well as the testis, when it was involved — was finally removed surgically. For this reason, and also to remove foci of tuberculous infection in the body, operation was performed in all these cases.

The technic used was as follows. If a draining sinus existed, a panel of skin was cut so as to surround the sinus with a good margin, and this incision was deepened down to the epididymis so that the panel of skin containing the sinus came away in one bloc when the epididymis was removed. The same procedure was frequently followed when the epididymis was adherent to an area of the scrotal skin, the adherent skin being removed with the epididymis. When the scrotal cavity had been entered the vas deferens was isolated near the epididymis, sectioned with a knife and treated with carbolic acid. The upper end of the vas was freed from the rest of the cord up to the external inguinal ring and then brought out without tension through a tiny stab wound about 2.5 cm lateral to the base of the penis, where it was fixed with a suture so that about 1 cm projected beyond the skin, any excess of vas being resected. The lower part of the vas and

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the vas at the time of operation. In this group of cases there were no deaths following epididymectomy or epididymo-orchidectomy.

SUMMARY

The incidence of pulmonary to genitourinary tuberculosis among soldiers in the Army seen at Fitzsimons General Hospital in 1945 was approximately 33.1. Negroes and American Indians had a high incidence.

Two main forms seen were renal tuberculosis and tuberculosis of the epididymis, the latter being more frequent in a ratio of 4:3. Both forms occurred in about a third of the cases.

Only about 20 per cent of the soldiers with genitourinary tuberculosis had demonstrable pulmonary tuberculosis, which was found twice as often in association with renal as with epididymal tuberculosis.

In these soldiers, since the renal tuberculosis was discovered in an early stage the first symptoms were mild — backache, some frequency and symptomless pyuria.

Retrograde pyelograms were more reliable and informative than intravenous pyelograms, but often all pyelograms were inconclusive and cultures had to be depended on to make the diagnosis of tuberculosis.

Nephrectomy was the treatment for unilateral renal tuberculosis. Soldiers withstood operation well, wound healing was good, and there were no deaths.

Epididymal tuberculosis was bilateral in a quarter of the cases. Scrotal abscess that had ruptured spontaneously, followed by persistently draining sinuses had occurred in more than a third of cases before hospitalization. First symptom was usually gradual, slightly painful swelling of the epididymis, which became large, hard and irregular. Epididymectomy, preserving the blood supply of the testis, was the treatment of choice. The wounds healed well, and there was no mortality. Exteriorizing the upper end of the vas deferens on the skin, so that it can drain there rather than inside the scrotum, is of real value.

The value of a prolonged period of hospital rest both before and after surgery cannot be overestimated. This results in improvement in the patient's general condition and resistance to tuberculosis, so that surgery is better tolerated and is less apt to spread the disease, and wound healing is better, with less tendency for chronic draining sinuses to develop.

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cystitis and also removes a tuberculous focus from the body. If active pulmonary tuberculosis existed, nephrectomy was not done until the process in the lung was arrested or quiescent to a point where operation was no longer contraindicated. In fact, in such cases, operation was considered desirable to remove a tuberculous focus from the body.

The type of operation done was the ordinary lumbar nephrectomy. The healing was so satisfactory in practically all cases that there seemed to be no object in doing a nephroureterectomy, especially since this procedure would have entailed another incision and put the patient through a more serious operation, increasing the likelihood of morbidity and mortality. In most cases the ureter was simply ligated, carbolyzed and dropped back into the wound. In some cases in which the ureter was dilated, thickened, tortuous and obviously diseased, it seemed better insurance against chronic sinus formation in the nephrectomy wound to bring the upper end of the remaining ureter out through a tiny stab wound below the main wound. In these soldiers as a group, however, the renal tuberculosis was discovered in an early stage and there were comparatively few of the dilated, thickened and tortuous ureters seen in advanced renal tuberculosis. The wounds were drained with soft rubber drains for twenty-four to forty-eight hours to let out serum, after which the drains were removed, because it was believed that leaving them in might help create a chronic sinus. Most of the nephrectomies were done under spinal anesthesia, which had the advantage that the patients could start taking frequent deep-breathing exercises immediately after operation as a prophylaxis against such pulmonary complications as atelectasis. For the same reason, the patients were made to lie with the operated side down for much of the time for the first twenty-four hours. If the spinal anesthesia wore off during the operation, it was supplemented with a small amount of Pentothal Sodium intravenously. To avoid thrombophlebitis, the patients were allowed out of bed beginning the day after operation, in fact, they occasionally stood up beside the bed on the evening of the operation, to try to void in a more natural position. Despite the fact that the patients continued to get out of bed every day beginning the day after operation, no weak or bulging scars resulted. No wounds broke down, although in 1 case much of the skin incision broke open. There were several cases in which a small draining sinus persisted for weeks. Almost to a man the patients withstood nephrectomy well, and there were no postoperative deaths in the twelve months ending in December, 1945.

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MEDICAL PROGRESS

ACUTE PULMONARY EDEMA, WITH SPECIAL REFERENCE TO EXPERIMENTAL STUDIES*

PHILIP H. HENNEMAN, M.D.†

BALTIMORE

THERE are many discrepancies between clinical observations, modes of therapy and the conventional explanations of the pathogenesis of pulmonary edema. Even superficial consideration reveals the inadequacies of the accepted explanations for this striking syndrome. In 1941 an editorial called attention to this problem, as follows: "Unfortunately as experimental and clinical observations on pulmonary oedema have accumulated it has become clear that the validity of the 'back pressure' or 'left ventricular failure' theory can no longer be considered as established."¹

DEFINITION

Acute pulmonary edema is a syndrome characterized by rapid flooding of the lung alveoli with a serous or serosanguinous fluid, it occurs in a great variety of clinical states, and may rapidly jeopardize the life of the patient.

Its nonspecific name has led to confusion with cardiac asthma, paroxysmal dyspnea or paroxysmal nocturnal dyspnea and chronic pulmonary edema. Cardiac asthma is constantly associated with heart disease, ancillary signs of congestive failure and asthmatic wheezes throughout the chest are usually present. Paroxysmal dyspnea, a closely related symptom of pulmonary congestion found in heart disease, usually appears at night and seems to be the same as cardiac asthma except for the associated bronchial constriction. Chronic pulmonary edema is found in congestive heart failure, pericapillary edema is rather constant, and the condition is rarely characterized by the explosive onset often found in acute pulmonary edema. The hyperneic phases of periodic breathing or Cheyne-Stokes respiration are easily differentiated from the syndrome under consideration, the former's name discloses the differential point involved. In spite of this apparently easy differential diagnosis, acute pulmonary edema is frequently confused both in the literature and clinically, and often must appear in its full-blown state before proper therapy is instituted on the basis of exact diagnosis.

INCIDENCE

Luisada² has reviewed the literature of acute pulmonary edema. There is no satisfactory report on

the incidence, and since patients often do not primarily from this condition, even hospital statistics are not entirely relevant. Such figures greatly needed, however. It is to be hoped that material from both adult and children's hospitals be included in such a review, since heart disease is far less frequent in the latter.

Reid and Teel³ state that pulmonary edema frequent immediate cause of death in cases of convulsive toxemia. Nessa and Rigler,⁴ in 1941, lected a series of 110 post-mortem cases of pulmonary edema in which the average age was fifteen years, with a variation from three months to eighty years. The primary cause of death was carcinoma in 17 cases (16 per cent), vascular accident in 20 (18 per cent), renal disturbance in 8 (7 per cent), cirrhosis and acute degeneration of the liver in 5 (5 per cent), blood dyscrasias in 4 (4 per cent), burns in 4 (4 per cent), septicemia in 4 (4 per cent), miscellaneous in 22 (20 per cent), and various surgical procedures in 26 (24 per cent). The percentage of surgical deaths is particularly notable in this series. Farber⁵ states that acute pulmonary edema is one of the most frequent causes of death found at autopsy in infants and children.

DESCRIPTION OF THE ATTACK

An excellent clinical description has been provided by Sir Thomas Lewis,⁶ as follows:

"The onset may resemble exactly that of the attacks previously described, occurring usually at night and waking the patient from sleep, or it may come in the hours of daylight and wakefulness. The separation of these attacks from those previously described (cardiac asthma) is in fact arbitrary and necessitated only by the relative dryness of the latter and their frequent repetition. In frank pulmonary oedema, while breathlessness is usually urgent from the start, cough is more prominent, and frothy blood-tinged sputum is freely or profusely expectorated. The marching events are often speedy. Cyanosis deepens rapidly, breathing becomes progressively more urgent and less effective. The attack may last at its height for hours. In fatal attacks the pulse becomes steadily weaker until imperceptible, the veins swell, and breathing becomes more gasping, infrequent, and then weaker until it ends."

In a fulminating form, the oedema occurs so rapidly and is so intense that, within a minute or two of crying out in fear, the patient is drowned by the copious blood-tinged fluid that pours into the respiratory passages and overflows frothing from the mouth and nose.

ROENTGENOLOGIC FINDINGS

Nessa and Rigler,⁴ in a discussion of the x-ray picture, refer to the classic butterfly-shaped, faint

*Presented before the Boylston Medical Society, January 16, 1946.

†Formerly, fourth-year student, Harvard Medical School.

symmetrical density of both lungs that is greatest at the hilus and gradually fades out toward the periphery, the apexes and extreme bases are usually clear. The density is homogeneous and obliterates all structural detail in the lung. The fluid collects in groups of alveoli, resulting in an irregular stippled density on the roentgenogram. The edema is often predominantly on one side or entirely unilateral. The condition is distinguished from pulmonary congestion by the presence of enlarged hilar shadows and dilated vessels throughout the lung fields and is further distinguished from massive atelectasis by elevation of the diaphragm, shift of the mediastinum and collapse of the chest wall. Lateral films revealed the congestion and edema to be central and not peripheral, in contrast to the congestion in pneumonia, which is usually peripheral in onset.

PATHOLOGY

Farber⁷ and Moon⁸ described the pathology of pulmonary edema, the former observing the same pathological findings in rabbits following cervical vagotomy. There were massive pulmonary edema, often with bloody fluid, and slight dilatation of the right ventricle and auricle. Pulmonary edema was present in the air and interstitial spaces, the former showed albuminoid casts and linings. The veins, capillaries and lymphatics were tremendously dilated, and the arterioles moderately so. Under direct vision in his experiments, Farber saw first the appearance of red petechiae of consolidation on the surface of the lung, with later enlargement and terminal dilatation of the right side of the heart. These changes in the heart, which have long been a source of controversy, are often explained as a result rather than a cause of the pulmonary edema. Undoubtedly, with such massive edema, obstruction to the flow of blood follows, pulmonary arterial pressure rises,⁹ and dilatation results, for the right side of the heart is working against a greater bed of fluid. Similarly, if a great amount of fluid is rapidly lost into the lungs, one might expect decreased return to the left side of the heart, with consequent decrease in size. Earlier workers sought to explain the dilatation frequently seen by failure of the right side, but it is difficult to understand how such failure could cause congestion of the lungs.

The fluid of pulmonary edema is usually characterized as a plasma filtrate with a high concentration of protein. Blood is found in varying amounts. Renault and de Basch¹⁰ demonstrated the absence of fibrin and inability to clot in pulmonary edema fluid. Pesenco¹¹ reported a vasodilatory effect that he believed to be due to the presence of histamine in large quantities.

PATHOLOGIC PHYSIOLOGY

Several features of the pathologic physiology of acute pulmonary edema are worthy of note.

Vicious circle of anoxia It is an old maxim that anoxia begets anoxia, and this is especially true of the lungs, for with the onset of anoxia there is increased capillary permeability and resultant pulmonary edema. In turn this edema prevents aeration of the alveoli and oxygenation of the blood, promoting and advancing the anoxia and edema. Drinker¹² presents many graphic illustrations of the drastic effect of anoxia on the lung capillaries and comments on their special susceptibility.

Ineffectual drainage Drinker¹² refers to the inadequacy of lymphatic drainage to clear pulmonary exudates and transudates. He points out three routes of removal: the bronchi and trachea, reabsorption and enzymatic digestion and resorption of the smaller molecular compounds.

Rise in venous pressure Many authors mention a rise in venous pressure with attacks of acute pulmonary edema, accepting this as evidence of a failing heart, with so-called "back pressure," and tacitly regarding cardiac failure in an acute and unusual form as the cause of acute pulmonary edema. Schmidt¹³ reports that positive intrathoracic pressures as high as 100 mm of mercury may be obtained during forced expiration, such as that in asthmatic breathing. Such a heightened pressure impedes venous return from the head, leading to dilated neck veins. With the respiratory obstruction of massive edema, dilated neck veins may well represent no more than a heightened intrathoracic pressure during expiration.

Blood-pressure changes Frugoni¹⁴ summarized the literature in 1931 and concluded there was no characteristic change in blood pressure with these attacks. Pulmonary edema of itself may well introduce changes in arterial tension. Schweigk¹⁵ and Parin¹⁶ demonstrated a reflex lowering of systemic arterial pressure, with an increase in pulmonary-artery pressure, that might explain some of the changes seen. Asphyxiation causes first a rise and later a fall in blood pressure, and many of the patients are certainly suffering from asphyxiation. Fishberg¹⁷ states there is a primary fall in blood pressure, followed by a rise, with anoxia. Lambert and Gremels,⁹ in Starling's Laboratory, noted in their experiments on heart-lung preparations that the pulmonary pressure in edema rose to high levels in the absence of cardiac failure.

Dyspnea Since dyspnea is such a prominent part of acute pulmonary edema and related conditions it is advantageous to review this subject by means of Altschule's¹⁸ schematic chart of some of the factors producing dyspnea in congestive failure (Fig. 1). It will be noted that most of the factors here involved are also involved in acute pulmonary edema.

General circulatory changes Subsequent to the onset of pulmonary edema there is a loss of a great quantity of fluid into the lungs, with resultant depletion of the circulating blood volume. The small, rapid, thready pulses noted by clinicians in

the late stages may well represent the onset of true shock. A rise in the hematocrit is frequently seen and is also due to loss of plasma into the alveoli.

Heart-lung preparations Many investigators have observed pulmonary edema in heart-lung preparations but have attached varying significance to the factors involved. Modrakowski,¹⁹ Matsuoka²⁰ and others emphasized the critical levels of the pulmonary arterial or general venous pressures necessary for the appearance of the pulmonary edema. Lambert and Gremels⁹ and Wiggers²¹ considered such pressures to be beyond the physiologic range. Lambert and Gremels⁹ and Newton²² observed that such preparations caused degenerative changes in

anoxemia of pulmonary edema, however, there may be increased venous return and increased cardiac output.²⁵ It is well known that a decreased velocity of peripheral and pulmonary blood flow occurs in patients with congestive failure,²⁶ but systematic investigations of the cardiac output by the newer methods and circulation times in patients with pulmonary edema have not been performed, probably owing to the serious nature of the paroxysms.

The urine There are many references in foreign reports to abnormalities of the urine following attacks of pulmonary edema. Some authors have even claimed that the albuminuria often noted is due

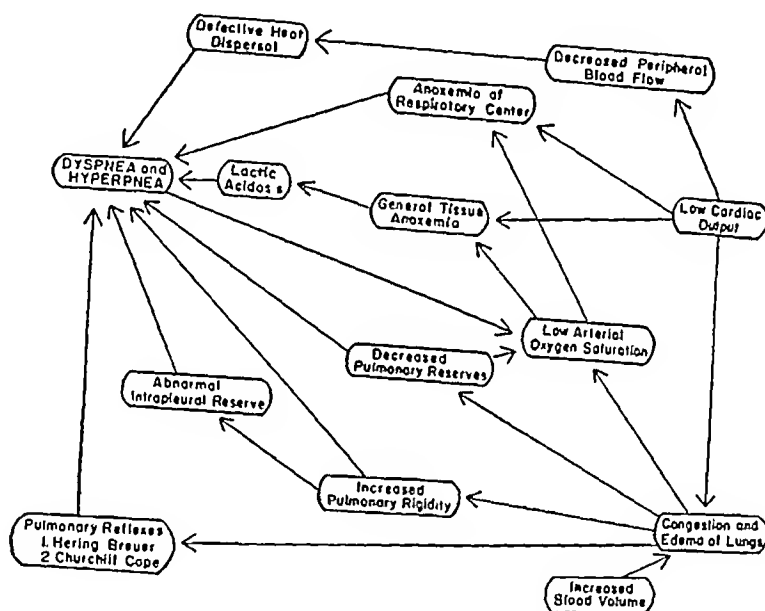


FIGURE 1 Factors in the Dyspnea of Chronic Cardiac Decompensation (Altschule¹⁴)

the intima of the lung capillaries, the edema being attributed principally to injury to the capillary endothelium and the greater permeability thereby produced. The toxic action of old defibrinated blood used in heart-lung circulations is well known. Thus the place of such preparations in pulmonary edema remains uncertain.

Cardiac output and circulation time Harrison,²³ in a review of the studies on cardiac output in cardiac asthma and acute pulmonary edema, states the following: "The idea that cardiac asthma is precipitated by increase in the cardiac output (due to decreased sympathetic activity during sleep, decreased peripheral resistance and hence increased venous return) has not been supported by recent work." In fact, the peripheral circulation has been found to be essentially normal, with no constant changes in cardiac output.²⁴ With the onset of the

to the resorption of albumin from the alveoli after the attack. Frugoni¹⁴ studied this problem and came to the conclusion that any urinary abnormalities merely reflected the underlying disease and were not characteristic of or caused by the attack of acute pulmonary edema.

ETIOLOGY

In the literature no lengthy studies on the incidence of pulmonary edema have been reported, and it is only recently that cases of obviously neurogenic origin have attracted the attention of English and American observers. Cases of cardiovascular disease appear to be predominant, but there are probably more cases of obviously neurogenic origin than has heretofore been appreciated. The variety of cases alone should throw some doubt on a mechanical or cardiac origin of this syndrome.

Cardiovascular diseases Types of cardiovascular diseases presenting this syndrome are as follows: aortic regurgitation and aortitis²⁷⁻³⁰, angina pectoris³⁰, coronary thrombosis^{27 30}, pericarditis^{29, 30}, mitral stenosis²⁹⁻³¹, cardiac failure^{17 31}, hypertension³⁰, wounds of the heart²⁹, and cardiac aneurysm²⁹

Toxic gases^{30, 32 33} Carlisle³³ gives the following list of the industrial gases that cause pulmonary edema: oxides of nitrogen, phosphorus oxychloride, phosphorus pentachloride, phosphorus trichloride, methyl bromide, chlorine, cadmium and dust from certain alkaloids

Drowning^{30, 34} Luisada³⁴ mentions drowning or the penetration of sea water into the upper respiratory passages as a cause of pulmonary edema. It is interesting to note that the lungs of drowning people do not contain sea water but rather the albuminous plasmalike fluid found in other cases of pulmonary edema

Uremia^{17, 27 29 30 35 36} Teisser²⁹ remarks on the frequency of acute pulmonary edema with nephritis and nephrosclerosis and the rarity of the syndrome in pure epithelial nephritis. He mentions gout as another cause, and regards the degree of renal insufficiency as determining the severity of the attack of pulmonary edema. Fishberg¹⁷ believes that the pulmonary edema of renal disease is due to accompanying cardiac weakness

Pregnancy and toxemia of pregnancy^{3, 27 30 35} Reimann³⁰ noted the incidence of pulmonary edema during pregnancy and considered it more frequent in pregnant women than in those with primary cardiac conditions. Reid and Teel,³ who studied this problem extensively, remarked that pulmonary edema is often an immediate cause of death from nonconvulsive toxemia. Among other measures they recommend rapid emptying of the uterus as part of the therapy

Paracentesis^{14, 29 30, 37, 38} Edema has been described following thoracic or abdominal paracentesis. In 1943, Vidal, Fourcade and Girard³⁸ reported that contralateral pulmonary edema was provoked by the creation of an extrapleural pneumothorax.

Central-nervous-system damage or disease^{27 31} The following conditions are cited as causes of pulmonary edema: intracranial hemorrhage^{34, 37 39}, insulin hypoglycemic coma^{40, 41}, brain tumor³⁹, head wounds and trauma^{30 34, 37 39 42-44}, diseases of the peripheral vagus^{39 45}, acute ascending myelitis^{29 30 34, 37 42}, tetanus²⁴, cerebral embolism and thrombosis^{30 37}, vertebral injuries^{37 46}, encephalitis^{37, 42}, polyneuritis and polyradiculitis³⁷, tabes dorsalis^{29 37}, lumbar puncture³⁷, phrenic-nerve crush under local anesthesia⁴⁷, cervical sympathectomy^{46, 48}, laminectomy⁴⁶, and emotional disorders and hysteria^{29 37}. Weissman,³⁹ in 1939, published an interesting series of 686 cases of intracranial hemorrhage with frequent pulmonary edema

In about two thirds of the cases the combined weight of the lungs was over 900 gm, whereas in the control group only 2 per cent of cases showed lungs of this size. Severe edema and congestion of the lungs developed almost immediately after intracranial hemorrhage — that is, within thirty minutes to an hour

Epileptic seizure Several reports list epileptic seizure as a cause of pulmonary edema^{30, 37, 39, 48-51}

Infections^{30, 31} The following infections are regarded as initiating pulmonary edema: acute rheumatic fever^{29, 42}, puerperal fever²⁹, typhoid fever^{29, 42}, measles⁵², scarlet fever⁴², and whooping cough⁵³. The acute circulatory changes described by Freedberg and Altschule⁵⁴ in the various phases of fever may also play a part in the pulmonary edema of infections

Toxic factors Teisser²⁹ reports cases of pulmonary edema in human beings associated with alcoholism and venoms, and in animals following the ingestion of potassium iodide, iodoform, pilocarpine and after intravenous injections of muscarine, chlorine, prussic acid, amyl nitrite and methyl salicylate. Reimann³⁰ lists among the toxic causes alcohol, barbital, iodine, morphine, epinephrine and asphyxiating gases. Bard⁵⁵ reported cases following muscarine poisoning

Miscellaneous causes Newmayer,⁵³ in 1907, reported pulmonary edema during the exertion of coitus and following shocking news. Gibbon and Gibbon⁵⁶ produced pulmonary edema in cats by lobectomy and plasma infusions and warned of clinical repetition of this danger. Other initiating factors are allergy,² thyroid storm,⁵⁷ beriberi⁵⁸ and reflexes from internal organs during operations. Bookhamer and Cullen⁵⁶ reported a case following manipulation of the stomach at operation for Banti's disease. Eason and Karp³⁵ mention angioneurotic edema and distention of abdominal organs. Fisher⁵⁸ reported a case of pulmonary edema, with anesthesia of the entire body as well as respiratory paralysis, following spinal anesthesia using 140 mg of Metycaine in 14 cc of water. Moon⁸ produced edema experimentally by intravenous muscarine, iodine, adrenalin in large amounts, serum in sensitized animals, perfusion of heart-lung preparations with old defibrinated blood, intravenous bile salts, in burns and intestinal obstruction. Most of these cases were observed in animals in shock. Moon⁸ and Reimann³⁰ commented on the frequency of pulmonary edema in shock, especially when death was somewhat delayed. MacKenzie and MacKenzie⁵⁹ found that thiourea and phenyl thiourea rapidly produced pulmonary edema in rats, and Drinker¹² mentions a simple thiourea compound that caused edema regardless of the route of administration. Choisy⁶⁰ reported a case of pulmonary edema with a hypertension apparently elicited by postmenopausal injections of steroids

ANATOMY AND PHYSIOLOGY OF HEART AND LUNGS

Control of Pulmonary Vascular Tone

The problem of pulmonary vascular tone has been disputed for years, and although a definite formulation has not been accepted by all workers the data are quite complete. De Burgh Daly⁶¹ stated that a complete understanding of the nervous mechanisms controlling the lung blood vessels is still lacking, but that workers who have analyzed and summarized the available data generally agree that such control exists. Olkon and Joannides,⁶² in 1930, observed under the microscope caliber changes of the alveolar capillaries in dogs, as well as localized hemorrhages on stress of hyperventilation and convulsions, and attributed their findings to vasomotor control over these vessels. De Burgh Daly and von Euler⁶³ showed that excitation of the stellate ganglion caused pulmonary vasoconstriction, whereas stimulation of the cervical vagi and the cervical or thoracic vagosympathetic nerves produced strong vasoconstriction in some preparations but weak vasodilatation in others. The results of experiments on dogs were summarized as follows:

In view of the finding by these workers that excitation of the thoracic vagosympathetic nerves may augment the mean effective pulmonary arterial pressure 40 per cent, a rise approximating to that obtained by occlusion of the main arterial branch to one lung, it would seem that the vasomotor nerves to the lungs may exert under certain conditions a profound effect on the pulmonary arterial pressure. If such profound changes occur normally the pulmonary vasomotor nerves may maintain a more or less constant pulmonary arterial pressure at all circulation rates, thereby preventing overloading of the right side of the heart.⁶⁴

Adrenalin raises pulmonary arterial pressure and in general constricts pulmonary vessels, although some reports deny such constriction.^{27, 61}

In general, acetyl choline causes vasodilatation of pulmonary vessels. Several workers have shown dilatation of arterioles and constriction of veins with acetyl choline.^{27, 61, 64}

De Burgh Daly and von Euler⁶³ demonstrated in experiments with eserine and atropine that pulmonary vasoconstrictor fibers in the rabbit belonged to the parasympathetic system. Similar pharmacologic evidence was presented by Berry and De Burgh Daly⁶⁵ in support of the presence of parasympathetic vasoconstrictor fibers running in the same nerves, as well as of sympathetic vasoconstrictor and dilator fibers in the thoracic vagosympathetic nerves of dogs, since the constrictor effect following excitation was suppressed or reversed by ergotamine tartrate. Kuré and his associates⁶⁶ described vasoconstrictors of the pulmonary vessels in the dog arising from spinal parasympathetic fibers in the dorsal spinal roots.

Luisada²⁷ raises the question whether vasomotor tone controls permeability of the pulmonary vessels and quotes Krogh's opinion that dilatation and permeability are parallel actions. Heidenhain and

Klemensieviez⁶⁷ claimed experimental proof of such direct vasomotor control of permeability.

In summary it can be said that there is vasomotor control of pulmonary vessels, probably with mixed action by both parasympathetic and orthosympathetic fibers. Adrenalin constricts the pulmonary vessels and acetyl choline dilates arterioles and constricts veins. Vasomotor control of permeability is a possibility.

Nerve Supply to Heart and Lungs

A brief review of the nervous pathways to these organs is included to demonstrate the pathways available for reflexes.

Miller⁶⁸ writes as follows:

The lungs receive their nerve supply from two sources: the vagi and the sympathetic nerves. Each vagus nerve, on reaching the back of the root of the lung, breaks up into numerous branches which, reinforced by fine branches from the second, third, and fourth thoracic ganglia of the sympathetic system, form the pulmonary plexuses. Each plexus gives off fibers which are distributed to the bronchi and pulmonary artery at the hilum. On entering the lung these fibers form two main plexuses which are distributed, one about the main-stem bronchus and its branches, the other about the pulmonary artery and its branches.

Another description of the nervous pathways is given by Karsner.⁶⁹

Larsell⁷⁰ concluded that the plexuses and ganglia of the human lung are in general similar to those described in the dog and rabbit. Afferent nerve endings are found in the bronchi as far as the proximal end of the alveolar ducts, in the atrial walls and in the bands of bronchial muscle, as well as in the adventitia of the pulmonary artery and the perichondrium of the bronchial cartilage plates. Terminations of motor type, which are present in the bronchial muscles and bronchial mucous glands, appear to arise from the nerve cells of the bronchial ganglia. Nerve fibers ending in the smooth muscle of the pulmonary and bronchial arteries originate from the periarterial plexus, which appears to be composed of postganglionic fibers from the upper thoracic sympathetic ganglia. Fibers from the periarterial plexus extend into the parenchyma and form a plexus of delicate nerve fibers on the pulmonary capillaries; terminal fibers end on the capillary walls.^{70, 71} The vagal efferent fibers arise from the dorsal nucleus of the vagus in the medulla and pass via the vagal trunk to be distributed over both lungs, their peripheral ganglia lying over the hilus of the lung. The vagal afferent pathways are again via the vagal trunk to the nodose ganglion lying just below the jugular foramen.²⁷

In 1926 Rasmussen⁷² described the nervous pathways as follows:

The sensory fibers of the vagus enter the upper portion of the medulla oblongata, where some terminate in the immediate neighborhood, while others run downward toward the spinal cord as part of the solitary fasciculus to end in various centers, especially the respiratory center. A few fibers may even go down into the spinal cord as far as the

first cervical segment (Cajal) Freeman in 1925 has also described a bundle of fine fibers as far as the third cervical segment.

The sympathetic supply to the lungs comes from the lateral horns of the spinal medulla via white rami from the second through the sixth thoracic ganglions. Most of the sympathetic fibers come through the stellate ganglion. Apparently the sympathetic supply is also distributed bilaterally to the lungs. There are also afferent pathways through these sympathetic fibers to the stellate ganglion and to the posterior horn cells of the cord via the gray rami.²⁷

Kur⁶⁶ claims to have demonstrated a spinal thoracic parasympathetic center and fibers, and although his work has not yet been confirmed¹³ some of his conclusions are of interest. He states that stimulation of fibers leaving the cord by the dorsal roots causes marked constriction of the pulmonary vessels of the dog, and that the spinal parasympathetic fibers therefore have a vasoconstrictor action on the lung while acting as vasodilators on the skin and viscera generally, the spinal center of the vasoconstrictors for the lung is situated in the thoracic region from the fourth to the eighth segments.

Cardiovascular Reflexes

Farber⁷³ in 1940, reported that rapid intravenous infusions in rabbits produced only moderate vascular congestion but after cervical vagotomy caused acute pulmonary edema.

Cervical vagotomy deprives the animal of the function of the nerve endings in the walls of the venae cavae and the pulmonary veins recently localized by Nonidez. The nerve endings in these locations are responsible for the acceleration of the cardiac rate induced by a rise in the pressure of blood entering the right auricle (the Bainbridge Reflex).

In recent experiments in dogs, Schweig¹⁴ found that branches of the pulmonary artery possess nerve endings responsible for reflex pressosensitivity. This mechanism regulates the cardiac rate and arterial vasomotor tone, an increase in the pressure within the pulmonary arterial system causes reflex slowing of the heart and vasodilatation, lowering of the pressure within the pulmonary arteries is responsible for opposite cardiovascular reactions. These reactions cannot be elicited if the nerve fibers from the pulmonary arteries which connect with the vagus nerves are severed. Schweig¹⁴ expressed the belief that during periods of pulmonary congestion the reflex lowering of the general blood pressure caused by a rise in the pulmonary arterial pressure is accompanied by peripheral and splanchnic vasodilatation, which tends to prevent overloading of the pulmonary circulation. It may be suggested also that at times of temporary increase in the pressure in the pulmonary artery such a mechanism might exert a beneficial influence on the pulmonary circulation by preventing an increase in pressure in the bronchial artery.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

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CASE 32421

PRESENTATION OF CASE

A seventy-eight-year-old retired electrician entered the hospital because of swelling of the legs

Ten months before admission the patient first began to have cramps in the right calf on walking short distances. Soon pains occurred in both legs, increasing in frequency and intensity until four or five months before admission, when they were more or less constant throughout each day. Occasionally the cramps also occurred at night during sleep. Three weeks before admission attacks of nocturnal dyspnea occurred at least once and later three or four times nightly. Associated with the attacks was a slight nonproductive cough. There had been no exertional dyspnea or anginal pain. There had previously been no history suggestive of cardiac difficulty. The patient had slept on two pillows for many years.

Two and a half weeks before admission swelling of the ankles and legs appeared for the first time. The legs were cool and red. Numerous small purple spots developed over the dorsums of both feet and the medial aspects of the calves. The swelling increased rapidly. Two weeks before admission spontaneous drainage of watery fluid from both legs began. The swelling extended slightly above the knee. There was no history of hypertension, headaches, tinnitus or visual disturbances.

Physical examination showed the patient to be moderately orthopneic. The neck veins just above the clavicle were engorged and pulsating in the up-

right position. The heart was enlarged, the border being 12 cm left of the midsternal line in the fifth interspace. The rhythm was irregular, and the rate was 120, with a pulse deficit of 20. No murmurs were heard. There were bilateral fine basal rales and decreased breath sounds, voice sounds and tactile fremitus. The liver edge extended 3 cm below the rib margin. Below the knees there was +++ pitting edema. The skin was tense, red, cool and dripping with moisture. There were purpuric spots and telangiectasis on the medial aspects of both thighs. No arterial pulsations were felt below the femoral vessels. The legs were not tender.

The temperature was 98°F, and the respirations were 20, the blood pressure was 160 systolic, 90 diastolic.

Examination of the blood showed 16 gm of hemoglobin and a white-cell count of 10,000, with 86 per cent neutrophils. A chest film showed moderate bilateral pleural fluid, widened pulmonary vessels and predominantly right-sided cardiac enlargement (Fig 1). An electrocardiogram was interpreted as showing auricular fibrillation, and enlargement and strain of the left side of the heart, without significant coronary disease. The circulation time (Decholin) was 29 seconds (normal, 12 to 18 seconds).

With bed rest and Purodigin the patient's condition improved rapidly, the rales disappeared and the swelling of the legs diminished markedly. The pulse remained irregular at 80 per minute. At 8.30 p m on the fifth hospital day mild, cramping, non-radiating pain suddenly developed in the lower abdomen. There was no nausea or vomiting. Six loose nonbloody bowel movements were passed with moderate but incomplete relief in the first hour after the onset of the abdominal pain. The abdomen was soft and nontender. Peristalsis was normally active, and there was no rebound tenderness. Rectal examination was negative. A stool specimen was guaiac negative. There was no liver or costo-vertebral-angle tenderness. The liver and spleen could not be felt. The lungs were clear. The blood pressure was 150 systolic, 90 diastolic, the pulse was 160 and regular. The temperature was 98°F. The white-cell count was 16,000, with 90 per cent neutrophils. A cardiette examination showed auricular flutter, with a 2:1 block. Six milligrams of morphine

and quinidine was given. There was little change during the night except for progressive apprehension and beginning disorientation. On the sixth hospital day, eleven hours after the onset of the attack, the patient was much worse, and could be roused only with difficulty. The temperature was 100.5°F, the pulse had dropped to 65, the respirations had risen to 40 and the blood pressure had dropped to 90 systolic, 40 diastolic. The white-cell count climbed to 26,000. The abdomen was markedly distended and moderately tender in both lower quadrants. There were no masses or rebound tenderness. Peristalsis was absent. No urine was passed. Twenty

The hemoglobin was slightly high and raises the question of polycythemia, but I assume that it was merely due to the accentuation of cardiac difficulties, with a certain amount of dehydration, and had no further significance. The prothrombin time was also elevated, but I doubt if it was important from the point of view of the final diagnosis.

Up to this point the case has been more or less a routine problem, and we are then presented with the final episode. At the time of this episode, I assume that the resident in charge of the medical wards thought that the patient was probably suffering from acute enteritis, and although a complete and care-



FIGURE 1

hours after the onset of the attack the patient was moribund and in deep shock, with a cold moist skin, an imperceptible blood pressure and Cheyne-Stokes respirations. He stopped breathing twenty-seven hours after the onset of the attack.

DIFFERENTIAL DIAGNOSIS

DR. CLAUDE E. WELCH: This case starts with a typical history of peripheral arteriosclerosis involving the legs. The swelling of the ankles and legs at a later time raises the question of whether the patient developed cardiac decompensation or whether he had a superimposed attack of venous thrombosis. "Two weeks before admission spontaneous drainage of watery fluid from both legs began." This implies the diagnosis of cardiac decompensation with edema, because such an occurrence with primary thrombophlebitis is extremely rare.

ful physical examination was indicated there did not seem to be any tremendous urgency about the case until the following morning. May I point out that if an examination is made immediately after the onset of an intra-abdominal surgical emergency, it may be almost negative and quite misleading. In other words, it takes a few hours for enough signs to develop to make a diagnosis. Hence, a great difference may be noted in the abdomen three hours after the onset of the illness or at the most six hours afterward. In the case under discussion there were progressive apprehension and beginning disorientation during the night. In the morning the patient was obviously a sick man and dying rather rapidly. At that time there was no indication for surgical help, the patient would merely have been speeded on his way.

The differential diagnosis, then, reduces itself to the question, What abdominal catastrophe could produce death in this short period of twenty-seven hours? There are only a few things that need be discussed mesenteric thrombosis, acute pancreatitis, dissecting aneurysm and volvulus. Several of them can be disposed of easily. In the first place, pancreatitis, which can rapidly produce shock and death, can be ruled out because there was no vomiting, all the symptoms were referable to the lower abdomen, and there was no tenderness at any time over the pancreas.

Dissecting aneurysm or some lesion of that type within the abdominal cavity can produce rapid death. Again, the history is unusual for that. The pain usually starts in the chest but later shifts to the abdomen. It would be of interest if we had had a report on the condition of the femoral vessels during the later examinations because if there is a dissecting aneurysm frequently one or both vessels become obliterated as time goes on. Again, with this diagnosis, pain should be steady.

Volvulus of the bowel could conceivably produce death in this short time, but it is unlikely. This would have been the first attack of volvulus—a rare occurrence in a man of seventy-eight. Usually there are repeated attacks before a fatal attack occurs.

By far the most attractive diagnosis is that of mesenteric thrombosis. There is nothing incompatible with that diagnosis. In the first place, the pain came on suddenly and was crampy. Crampy pain is not at all infrequent with mesenteric thrombosis, although the pain is often steady. The diarrhea is suggestive of involvement of the bowel. The physical findings at the onset are often as negative as they were in this case. I might mention that normal peristalsis is a misleading sign. Most of you know that again and again there can be acute inflammation or a vascular lesion in the abdomen with normal peristalsis. In the case under discussion, as time went on, shock developed, the white-cell count rose to 26,000 and evidence of peritoneal irritation appeared. All these signs are typical of mesenteric thrombosis. The fact that no urine was passed can indicate one or two things—either complete block of the renal artery by thrombosis, which is extremely unlikely with mesenteric thrombosis, or, much more probably, that the patient was in a state of shock.

If this was mesenteric thrombosis, what type was it? Could the patient have had an arterial embolus, or was it primary arterial or venous thrombosis? It is a difficult differential diagnosis to make. I might merely say that if venous thrombosis occurs as the primary incident, the symptoms are likely to last for several days before the case is considered a surgical emergency. On the other hand, if the obstruction is arterial in type, it is much more probable that the patient will either die or come to operation rapidly.

I doubt if this was an arterial embolus because the pulse was still irregular and the patient was still fibrillating at the time the pain started. If he had stopped fibrillating or had had other cardiac changes at that time, an embolus would be likelier. I think that this patient died of mesenteric thrombosis that was primary in the arterial system but at the time of autopsy involved both mesenteric arteries and veins.

DR. TRACY B. MALLORY: Do you want to see the x-ray films?

DR. WELCH: I did not know that there were any.

DR. MILFORD D. SCHULZ: I do not believe they contribute anything.

DR. WELCH: They might be of interest, but I should not change the diagnosis.

DR. ALLAN M. BUTLER: What would you have done on the ward? Would you have liked a plain film of the abdomen when the pain started?

DR. WELCH: Later on.

There is an x-ray picture described as being typical of mesenteric thrombosis. The scout film looks like intestinal obstruction running over to the splenic flexure. When a barium enema is given, however, no evidence of obstruction is found.

DR. SCHULZ: The film shows enlargement of the heart, engorgement of the hilar vessels, particularly on the left, and fluid in the pleural sinuses.

DR. LEWIS K. DAHL: I should like to ask Dr. Welch what he would have done if he had been on the ward and made the diagnosis of mesenteric thrombosis.

DR. WELCH: That is a difficult question to answer. In the first place, the man was seventy-eight years old and had to die sometime. I think that the surgeon must seriously consider whether postponing death is necessarily desirable or even justified. We know that this man was old and that in such case the operative mortality for mesenteric thrombosis is 90 per cent. But being a surgeon I should probably have advised operation, realizing that it would probably have killed him but might possibly have saved him temporarily.

CLINICAL DIAGNOSES

Arteriosclerotic heart disease

Cardiac failure

Mesenteric thrombosis

DR. WELCH'S DIAGNOSIS

Mesenteric thrombosis, arterial and venous

ANATOMICAL DIAGNOSES

Embolism, superior mesenteric artery

Arteriosclerosis, generalized, severe

Arteriosclerotic aneurysm of thoracic aorta, with mural thrombosis

Hypertrophy of heart

PATHOLOGICAL DISCUSSION

DR MALLORY The immediate cause of death in case was occlusion of the mesenteric artery. It not due to local thrombosis, however, but to an embolus. The source of the embolus was not in the heart. It was a large fusiform arteriosclerotic aneurysm of the thoracic aorta. I was hoping that Dr Schulz would show that to us.

DR SCHULZ What I took to be part of the left aortic root is the aneurysm.

DR MALLORY The aneurysm measured 13 cm in length. It was partially filled with an adherent, gelatinous clot. The clot found in the superior mesenteric artery was of the same color and consistency as that in the aorta and was not adherent. It would have been if formed locally, I therefore think that we can be reasonably sure that it was an embolus. The other findings were not of any particular significance. There was widespread generalized arteriosclerosis, the heart was slightly hypertrophied, and the majority of the other organs showed only senile atrophy, which would be expected in the age of seventy-eight.

CASE 32422

PRESENTATION OF CASE

A sixty-six-year-old watchman entered the hospital because of painless hematuria.

The patient had his first attack of hematuria three months before entry, when he was taking sulfonamides for an upper respiratory infection. The attack lasted for four days. The patient then remained asymptomatic until three weeks before entry, when he had another entirely spontaneous episode lasting one day during which he passed grossly bloody urine and clots, there was no pain with the bleeding. He was seen at that time in the Out Patient Department, where cystoscopy showed the blood to be coming from the right ureter. An intravenous pyelogram revealed a reduplication of the right urinary passage, with the point of reduplication not demonstrable. One ureter entered the middle and lower calyces, and the other led to the upper calyx. The minor calyces, particularly the lower, were incompletely visualized, and there was a questionable filling defect. The urinary passages on the left side were normal. There was an irregular, filling defect along the floor of the bladder over the region of the prostate, and at least one small diverticulum on the left side of the bladder. The patient had had no other urinary symptoms and passed a good stream. He had had no chills or fever and had recently gained 4 pounds.

Seven years before entry the patient was in another hospital because of a "cavity in the right lower lobe." Healing was apparently spontaneous,

and he was discharged in three weeks. During the following six years he suffered from pain in the right chest whenever he caught cold. He was seen in the Medical Out Patient Department six months before admission, when a chest x-ray film showed increased density in the region of the right apex and first interspace that was interpreted as probably inactive tuberculosis.

Physical examination was negative except for a boggy, nontender prostate, enlarged to about twice the normal size.

The temperature, pulse and respirations were normal. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,450,000, with 80 per cent hemoglobin, and a white-cell count of 9700. The nonprotein nitrogen was 30 mg and the total protein 6.4 gm per 100 cc, and the chloride 101 milliequiv per liter. The prothrombin time was normal. The urine was light amber and acid, and had a specific gravity of 1.012, it gave a ++ test for albumin, and the sediment contained 20 red cells and 4 white cells per high-power field. A culture and smear were sterile.

An x-ray film of the chest showed no change from the previous examination. A retrograde pyelogram revealed the reduplication on the right to be complete. The lowermost group of calyces were not unusual. In the upper group a filling defect was again seen, and there were two rounded areas measuring about 1.5 cm in diameter each, consistent with nonopaque stones or tumor (Fig. 1). A plain film over the region of the right kidney showed minimal flecks of calcification in the region of the upper pole in, and corresponding to, the location of the mass seen in the pyelogram.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR WYLAND F. LEADBETTER I do not know how much sulfonamide this patient was taking or whether he was taking sodium bicarbonate with it. There is a possibility that this therapy had a bearing on the subsequent events, but it is unlikely.

Painless hematuria in the presence of clots, particularly large clots, might be thought to be due to bleeding from the bladder, because bleeding from the kidneys, if massive and with clots in the renal pelvis, is quite apt to produce renal colic. That statement, however, ought not to be taken as a definite rule — simply something to bear in mind.

It is impossible to make a definite diagnosis from the intravenous urograms. The record simply states that the urinary passages on the left were normal. Therefore, we can say that this patient presumably had hematuria coming from the right upper urinary tract, but we do not know whether it came from the upper or lower half of the right kidney.

At cystoscopy there was no mention of a tumor of the bladder. The irregular filling defect, I sup-

pose, was visualized from the cystogram. The fact that there was a diverticulum suggests that there was or had been some obstruction to the lower urinary passage.

The lung cavitation is interesting. It seems unlikely that that was a tuberculous infection. It was possibly a lung abscess that healed. I can not see that it had any bearing on the present situation.

White cells in the urine could be associated with the bleeding and need not be an indicator of infection.

The retrograde pyelogram should be the key to the diagnosis in this case, and we might see the films now.

DR. MILFORD D. SCHULZ: This is a representative film, and the left side appears to be normal.



FIGURE 1

An x-ray film taken six months before admission showed inactive tuberculosis of the right upper lobe. That might have had a bearing on the present illness, but I do not believe that we can do much more than assume that this patient had had active pulmonary tuberculosis at one time.

The lower calyces and ureter on the right seem also to be quite normal, but there is something amiss in the calyx of the upper half. In the duplicated right kidney there is a round, lobulated filling defect that is better seen on the retrograde film.

LEADBETTER Is there any calcification in the area?

R. SCHULZ There is no calcification in that and the ureter leading to the involved calyx normal

R. ALLAN M. BUTLER There is no calcification, does that rule out a stone?

R. SCHULZ No, nor does it rule out tuberculosis

R. BUTLER Is the incompleteness of the filling the right upper half a possible indication of a lesion that is not radio-opaque?

R. SCHULZ It could be a nonopaque stone, blood clot, tumor or granulation tissue — anything that displaces the opaque material in the pelvic calyces

R. LEADBETTER May we see the film that outlines the ureter?

R. SCHULZ There is nothing remarkable about except that it shows the upper third of the ureter, which looks perfectly normal. There is a suggestion of a little more of the lower ureter on the right side, but there is nothing of further interest

DR. LEADBETTER Will you be willing to comment on the cystogram?

DR. SCHULZ The irregularity in the floor of the bladder looks as if it might be due to prostatic enlargement. The diverticulum is probably associated with the irregularities and trabeculations seen throughout the wall of the bladder.

DR. LEADBETTER This illustrates the point that when hematuria is present it is necessary to work the case up completely to determine accurately the site of bleeding and to obtain good pyelograms, if the upper urinary tract is involved. The history in this case was one of short duration, with two episodes of gross hematuria, and I think that we can definitely say that the bleeding came from the right urinary tract. In view of the finding in the upper half of the right kidney, we must assume that the bleeding originated there, although there is no direct statement to that effect. We may assume that there was benign prostatic hyperplasia, which accounts for the changes and the irregularities in the bladder floor and the diverticulum of the bladder.

What was the lesion in the upper pole of the right kidney? The x-ray studies show a definite filling defect, although it is not clearly outlined. The diagnosis seems to rest between tumor, tuberculosis and nonopaque calculi. There is one other point to be noted regarding the filling defect: it does not appear to be free in the pelvis. Whatever the lesion was, it was associated with calyces or with the parenchyma and was not free in the true pelvis. For that reason I should be inclined to rule out the possibility of nonopaque stone. If

we were more critical about this pyelogram we could say that this shadow represents the upper calyx, and these, the lower and midcalyces in the upper portion of the kidney. There appears to be dye extending up about the filling defect and possibly representing infiltration of dye into the kidney substance. This is somewhat suggestive of renal tuberculosis. On the other hand, we are dealing with an illness of short duration and the ureter appears normal. In renal tuberculosis the ureter usually shows characteristic changes, and I am inclined to think that one is obligated to make a diagnosis of renal tumor.

DR. BENJAMIN CASTLEMAN Would the shadow be round if it were due to tuberculosis?

DR. LEADBETTER Not usually, but I think one can find almost anything in a cavitation due to tuberculosis. On the basis of the history and the x-ray findings I believe that one must make a diagnosis of tumor involving the upper pole of the kidney. It is necessary to differentiate papillary tumor of the pelvis and renal-cell carcinoma — that is, a tumor originating in the renal parenchyma. It is difficult to decide in this case. The outline of the kidney is not definite in the films, but it is fairly obvious that there is no enlargement of the upper pole of the kidney, and it is probably better to make a diagnosis of papillary carcinoma of the renal pelvis, involving the upper half of the right kidney, benign prostatic hyperplasia and, in addition, inactive tuberculosis of the right upper lobe of the lung.

DR. JAMES B. TOWNSEND How often will tuberculosis reveal itself as painless hematuria?

DR. LEADBETTER Quite often, it is one of the most frequent signs of early renal tuberculosis. On the basis of the pyelogram showing the essentially normal ureter it is difficult to make a diagnosis of renal tuberculosis.

DR. TOWNSEND I suppose that efforts were made to do guinea-pig inoculation.

DR. CASTLEMAN I do not believe that they waited that long.

DR. BUTLER This summary does not tell anything about what was found in the urine by ureteral catheters at the retrograde cystoscopic examination. With catheters up the two ureters on the side where disease was suspected and with catheters up the ureter on the side where no disease was suspected, one had a wonderful opportunity to see what kind of urine was coming from each portion of the kidney. Was any such information obtained?

DR. CASTLEMAN Yes, the material was both cultured and injected into a guinea pig.

CLINICAL DIAGNOSIS

Tumor, upper pole of right kidney

DR LEADBETTER'S DIAGNOSES

Papillary tumor, right kidney pelvis, involving
upper half of double pelvis
Benign prostatic hyperplasia

ANATOMICAL DIAGNOSIS

Papillary carcinoma (Grade II A), involving
upper half of bifid pelvis

PATHOLOGICAL DISCUSSION

DR CASTLEMAN At operation the lesion proved to be a papillary carcinoma, which was graded as II A. As Dr Leadbetter predicted, it was attached to the pelvis and extended into the calyx for a short distance. The ureter was removed at the same time because papillary tumor was suspected. The patient made an uneventful convalescence and was seen a month or two later.

DR LEADBETTER Was the whole kidney removed?

DR CASTLEMAN The entire kidney was removed, the lower calyces showed petechial hemorrhage—I assume from operative trauma. There was nothing in the lower half.

DR LEADBETTER I think it would be possible to remove only the upper half if one could be sure of the diagnosis, and I think that if one could visualize the pelvis it might be possible to make the diagnosis.

DR B. T. TOWERY Were there any ureteral implants?

DR CASTLEMAN No.

DR BUTLER Would it not have been an advantage to take a lateral film at the time of either the intravenous or retrograde pyelograms?

DR SCHULZ I do not know about this case, but lateral films taken at the time of retrograde pyelography are often helpful, especially in the demonstration of tumor.

DR BUTLER That is why I thought that when the possibility of tumor is suspected it would be justified.

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SALVATION ARMY LOOKS AHEAD

THE Salvation Army was founded in London in 1864 by William Booth to carry out "the fundamental purpose of taking the Gospel to those who need it but will not seek it." After eighty-two years this evangelistic organization, functioning as the world's greatest system of social services, carries on its work and has its headquarters in every country on the face of the globe. It is infinite in its capacity for mercy, its doors are closed to no one, it works in its own centers and in its hospitals, it finds room for its services in the home and in the street, in the church and in the prison cell.

This month the Salvation Army of Greater Boston is asking for a million dollars. The sum is greater than its usual request because, in addition to its

customary and postwar services, it must have \$149,000 for remodeling of five corps centers and \$375,000 for a new Evangeline Booth Home and Hospital.

The Evangeline Booth Home and Hospital of Boston, one of thirty-five similar institutions operated by the Salvation Army in this country, was opened as a home in Dorchester in 1892. In 1900 it moved to larger quarters, and the hospital department was established, twenty years later, when it entered its present quarters on West Newton Street, the hospital department was separated from the home department and reorganized as a regular maternity hospital equipped to receive patients of the medical staff.

The home cares for unwed mothers regardless of multiparity, the hospital, in which 764 babies were delivered in 1945, is an obstetric teaching unit of Tufts College Medical School, approved by the American Medical Association and the American College of Surgeons. It also conducts a training school for attendant nurses. During the war the hospital was made available to medical personnel of the United States Coast Guard for the delivery of Coast Guard wives.

A general improvement in hospital standards combined with a desire to give increased and better service has forced the Evangeline Booth Home and Hospital to the decision to abandon its present inadequate quarters. It now needs a lying-in hospital of eighty to a hundred beds, with a separate building for the home department, and is asking the public to provide funds to fill this need, even in a year when larger hospitals are experiencing growing pains and are expressing their own needs for expansion. It may be taken for granted that the people of Greater Boston, among their other commitments, will continue to support this essential charity.

RADIOACTIVE IODINE IN THE TREATMENT OF THYROTOXICOSIS

AMONG the recent significant contributions of physics to medicine are studies with radioactive iodine. Dr. Saul Hertz, working in collaboration with Drs. Arthur Roberts, Robley Evans, William Salter and others, utilized this isotope in studying some fundamental mechanisms of function of the thyroid gland, especially those concerned with

iodine metabolism In 1942, Hertz and Roberts,¹ and also Hamilton and Lawrence,² rendered preliminary reports of the effects of therapy with radioactive iodine in the treatment of thyrotoxicosis The results encouraged an extension of the studies by Hertz and Roberts³ On the basis of these observations, Chapman and Evans⁴ were prompted to use larger doses of radioactive iodine than previously had been used in thyrotoxic patients

The basis for such therapy arises from the fact that, since in untreated hyperthyroidism the thyroid gland can take up as much as 80 per cent of a small dose (less than 2 mg) of iodide within a few hours after its administration, it is possible to obtain concentrated irradiation at the site desired without undue exposure of other tissues Although the total number of patients treated with radioactive iodine is relatively small, the results of this type of treatment appear encouraging Hertz and Roberts³ report that, in 29 uninodized patients with hyperthyroidism whose goiters weighed from 60 to 75 gm, radioactive iodine in doses of 5 to 25 millicuries cured the disease in about 80 per cent Chapman and Evans⁴ observed that, in 22 patients with hyperthyroidism whom they treated with larger amounts (14 to 52 millicuries) of radioactive iodine, 14 responded well to the single dose Three were given two doses, and 5 were given three doses, and as a rule, the subsequent doses were larger than the first one Four patients later developed myxedema, and 2 had a persistence of thyrotoxicosis following treatment, although the disease became less intense

The chief problem in the use of radioactive iodine is to determine the optimal dose The amount required depends on the amount of iodine in the body, the size of the thyroid gland, the nature of the pathologic changes in the gland and many other conditions Inability to estimate these factors accurately makes it more difficult to select the proper dose than it is for the surgeon to decide how much of the thyroid tissue should be removed In either instance, only a slight difference in the number of cells that are permitted to live may result in a persistence of the thyrotoxicosis or the development of myxedema It appears wise to use a minimal dose of radioactive iodine, since additional doses can be given if needed, with excessive therapy some patients may develop permanent myxedema Few

other ill effects from the use of radioactive iodine therapy have been observed Occasional patients have had transient reactions resembling roentgen-ray sickness Whether this type of treatment predisposes to the development of cancer or whether structural damages will subsequently occur in other tissues remains to be ascertained

The extent of usefulness of this form of therapy has not been determined In certain complicated cases it is unquestionably the treatment of choice Moreover, it appears to be useful in some patients who have been unsuccessfully treated with thiouracils and in those who have not obtained good results after having been subjected to surgical treatment Indeed, it is possible that this form of therapy may become the one of choice in the majority of patients with thyrotoxicosis, but this can be established only on the basis of the findings in extended investigative studies

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NOTICES

NEW ENGLAND PEDIATRIC SOCIETY

A meeting of the New England Pediatric Society will be held on Wednesday, October 23, in Boston

PROGRAM

- 12 00 m Clinicopathological Conference of the Children's Hospital (held temporarily at the Peter Bent Brigham Hospital Amphitheater) Members of the Society are invited to attend
- 1 15 p m Luncheon at Vanderbilt Hall, Harvard Medical School (price, 70 cents)
- 2 00 p m Regular Combined Clinic Main Amphitheater, Children's Hospital
- 3 00 p m Presentation of patients with tumors Main Amphitheater, Children's Hospital Members of the medical profession and students are invited to attend.
- 5 30 p m Refreshments at Longwood Towers
- 6 30 p m Dinner at Longwood Towers (price, \$2.50, including tax) Members of the Society and their guests are invited to attend
- 7 30 p m Tumors in Infants and Children Children's Hospital Dr Sidney Farber Members of the medical profession and students are invited to attend

NEW ENGLAND ROENTGEN RAY SOCIETY

The New England Roentgen Ray Society will hold its first meeting of the season on Friday, October 18, at the Hotel Beaconsfield, Brookline, Massachusetts At 4 30 p m there will be an x-ray conference on diseases of the gastrointestinal tract At 8 00 p m Dr Frederic E Templeton, of Seattle, Washington, will speak on "The Esophagus — Some Roentgenologic Observations on the Muscular Action in the Normal and Abnormal" Interested physicians are invited to attend

(Notices continued on page xiii)

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SUBACUTE BACTERIAL ENDOCARDITIS*

A Report of Two Cases Successfully Treated with Penicillin

BENEDICT F MASSELL, M D,† AND T DUCKETT JONES, M D ‡

With the Technical Assistance of Mary Meyeserian

BOSTON

THE medical literature contains reports of many cases of subacute bacterial endocarditis treated with penicillin.¹⁻¹⁴ Nevertheless, we are prompted to contribute reports of 2 additional cases. In the first place, all carefully studied cases treated with penicillin should be reported irrespective of their therapeutic outcome,[§] so that by the accumulation of data on large numbers of cases, it will be possible to evaluate adequately the various aspects of this remarkable treatment and to explain the reasons for failure, which still occurs in about 25 to 30 per cent of cases. Secondly, certain features of these 2 cases show interesting contrasts and comparisons. Finally, the penicillin resistance of the *Streptococcus viridans* isolated from the blood in one of the cases was apparently greater than that of the originally isolated causative organism responsible for any other successfully treated case reported so far in the medical literature.⁶⁻¹⁴

CASE 1. G. T. (H. G. S. 6465), a 16-year-old girl, suffered her only definite attack of rheumatic fever at the age of 8 years. During this episode she was treated at the House of the Good Samaritan, and later she was examined periodically in the Out-Patient Department of the Children's Hospital and in the Rheumatic-Fever Clinic of the Massachusetts General Hospital. From the time of discharge from the House of the Good Samaritan until the onset of her last illness she remained essentially well except for occasional nosebleeds and colds. There was never any clinical evidence of acute rheumatic fever, and the blood sedimentation rate remained normal.

The present illness began on June 13, 1944, when the patient went swimming. Soon after arriving home, she had a chill. Chills continued off and on for 2 or 3 days, and migratory joint pains developed. Pains in the muscles of the right upper arm also occurred. There was no history of tooth extraction or other dental work and no respiratory infection prior to the onset of this illness.

On July 20 examination revealed an oral temperature of 103.2°F. The patient appeared thin and pale. The heart was borderline in size, the apex impulse being about in the midclavicular line. There was a loud systolic murmur at the

mitral area. There were no diastolic murmurs. There were no petechiae, but the spleen was easily palpable. Because of the enlarged spleen, subacute bacterial endocarditis was suspected.

Because of an unavoidable delay the patient was not admitted to the House of the Good Samaritan until August 25. During the 1st week at the hospital she was obviously extremely ill. The rectal temperature reached daily peaks of 102.5 to 104.5°F. At times she was lethargic, and sometimes she was delirious. There was moderate pallor. Several tender red spots appeared from time to time over the tips of the fingers and toes. The heart was of borderline size, and the rhythm was regular. The heart rate was rapid and varied from 110 to 140 per minute. There was a loud, widely transmitted, mitral systolic murmur. There were no diastolic murmurs. The abdomen was examined with difficulty because of marked tenderness and spasm in the left upper quadrant. After a few days the spasm lessened, and the spleen was definitely felt. The electrocardiogram was essentially normal except for sinus tachycardia. The PR interval was 0.16 second. The corrected sedimentation rate (Rourke-Ernstene method) ranged between 1.2 and 1.5 mm per minute.

Examination of the blood showed a red-cell count of 3,500,000, with a hemoglobin (photoelectric) of 9.4 gm., and a white-cell count varying from 9000 to 12,000, with 60 per cent neutrophils, 28 per cent lymphocytes, 8 per cent monocytes and 4 per cent eosinophils. The hematocrit reading was 33. The antistreptolysin titer was 125 units. The centrifuged sediment of a single urine specimen showed 5 red cells per high-power field, otherwise numerous urine specimens were negative. The specific gravity ranged from 1.017 to 1.030. Five successive daily blood cultures beginning on August 26 were positive for *Streptococcus viridans*. The organism isolated from these cultures was inhibited in vitro by as little as 0.02 unit of penicillin per cubic centimeter, even a heavy inoculum was inhibited by 0.06 unit.

Penicillin therapy was started on August 31. Intramuscular injections of 37,500 units were given every 3 hours, making a total of 300,000 units every 24 hours. This treatment was continued for 14 days. On September 14, the dose was reduced to 12,500 units intramuscularly every 3 hours, totaling 100,000 units every 24 hours. This reduced dosage was continued for 10 days, when the penicillin therapy was discontinued. During the 24 days of treatment the patient received a total of 5,000,000 units of penicillin. Penicillin blood levels were determined on several occasions on specimens taken 3 hours after the previous injection and just prior to the next injection. On all these occasions the concentration was less than 0.06 unit per cubic centimeter of serum.

The response to penicillin therapy was dramatic. Within 24 hours of the first injection the fever lessened, and the downward trend continued until September 6, when the rectal temperature failed to rise above 100°F. Thereafter the temperature remained normal except for an unexplained period in which the rectal temperature reached 102.5°F. This

*From the House of the Good Samaritan.

†Research associate, House of the Good Samaritan.

‡Research director, House of the Good Samaritan.

§No case of subacute bacterial endocarditis has been unsuccessfully treated with penicillin at this hospital.

febrile episode began on September 15, the day after the 24-hour penicillin dosage had been reduced from 300,000 to 100,000 units, but subsided within 3 days, and thereafter the rectal temperature remained well under 100°F. The patient began to feel better almost immediately after treatment was begun, and her general appearance improved rapidly. The tenderness in the left upper quadrant of the abdomen soon disappeared, but the spleen remained readily palpable until January 23, 1945. Thereafter it could be felt only occasionally just below the left costal margin. The frequency with which small, tender, red spots occurred on the fingers and toes lessened noticeably by September 13, 1944. Occasional spots continued to appear, however, as long as 3 months after the treatment was discontinued.

The corrected sedimentation rate gradually lessened but did not fall within the upper normal limit of 0.4 mm per minute until October 23, after which it remained well within normal limits. The anemia likewise improved, by November 13, the hematocrit reading was 43. The first blood culture after the onset of therapy was taken on September 2 and was sterile. Seven additional cultures during the course of penicillin injections and 32 others after termination of treatment were also sterile.

After discharge from the ward on February 11, the patient was examined at intervals of 1 or 2 months at the Follow-up Clinic and was last seen on September 25, 1946. During this entire period she was feeling extremely well, attending school and leading an essentially normal life. Physical examination remained entirely negative except for the cardiac findings, which had not changed. The corrected sedimentation rate was found to be well within normal limits (less than 0.4 mm per minute), and the blood cultures remained sterile. During the total follow-up period of 24 months since discontinuation of therapy, there was a total of forty-four sterile blood cultures.

CASE 2. M. A. (HGS 4432), a 27-year-old woman, was admitted to the House of the Good Samaritan for the first time on March 10, 1927, when she was 8 years old, during her only definite attack of rheumatic fever. Following discharge, she was entirely well and was able to lead a physically active life. She was examined on occasion in the Out-Patient Department of the Boston City Hospital until October 10, 1939. Thereafter follow-up examinations were continued at intervals at the House of the Good Samaritan clinic. On December 2, 1943, the heart was described as borderline in size, the apex impulse being in the 5th intercostal space 7.5 cm. to the left of the midsternal line and just about in the midclavicular line. The rhythm was regular. There was a fairly loud (Grade 3), somewhat harsh, systolic murmur maximum at the apex, where the mitral 1st sound was masked. There were no definite diastolic murmurs.

In May, 1944, without any preceding respiratory infection, tooth extraction or other unusual event, the patient began to feel tired and developed migratory joint pains. In spite of these symptoms she did not remain in bed for any long period until July 1, when the left ankle became swollen and so painful that she could not walk. About a week later she had lower abdominal pain and for the first time noticed fever, the temperature reaching 102°F (oral). Within a few days these symptoms subsided, but pain in the left buttock and in the left side of the chest soon developed. The chest pain was aggravated by deep breathing. An x-ray film revealed no abnormalities. Mild fever returned and continued in a variable fashion thereafter.

Examination of the patient at home on August 29 revealed an oral temperature of 99.6°F. Three small, nontender red spots and a tender area of purplish discoloration were seen on the extremities. The cardiac findings were essentially the same as those described at the last previous clinic visit on December 2.

A diagnosis of probable subacute bacterial endocarditis was made, and the patient was admitted to the House of the Good Samaritan on September 5. For a period of 23 days—from September 5 to September 28—during which therapy was withheld so that adequate observations could be made, the patient felt fairly well and did not appear very ill. There was a low-grade fever, the daily maximum rectal temperature varying from 100.2 to 101.0°F. Several petechiae appeared during this period. On the morning of September 28, prior to the initiation of therapy, a painful, tender, purplish discoloration, several centimeters in diameter, appeared over the 4th toe of the left foot. At no time could the spleen be felt.

The electrocardiogram was normal and had a PR interval of 0.14 second. The corrected sedimentation rate varied from 0.55 to 0.92 mm per minute. Examination of the blood showed a red-cell count of 3,800,000, with a hemoglobin (photoelectric) of 10.2 gm., and a white-cell count varying from 4700 to 8000, with 67 per cent neutrophils, 29 per cent lymphocytes, 1 per cent endothelial cells and 3 per cent eosinophils. The hematocrit reading varied from 31 to 33. The antistreptolysin titer was 200 units. Eight urine specimens were essentially negative and showed no evidence of microscopic hematuria, the specific gravity varied from 1.017 to 1.024.

Ten consecutive blood cultures taken prior to therapy consistently gave a pure growth of *Str. viridans*. In vitro studies showed that inhibition of growth of this organism required at least 0.40 unit of penicillin per cubic centimeter. With even high concentrations of penicillin, complete or nearly complete sterility could be obtained only if a highly diluted culture was used for the inoculum.

Penicillin therapy was begun on September 28. It was obvious from the in vitro studies that the causative organism was relatively resistant to penicillin and that, to obtain adequate blood levels, larger amounts of penicillin than had been customary at that time would be necessary. For the purpose of obtaining information concerning the relation of blood concentration to dosage, however, an initial daily dose of 240,000 units was given, and this was gradually increased to a maximum of 960,000 units by October 5. During these first 8 days of therapy the penicillin was given intramuscularly every hour in divided doses. On October 6 the method of administration was changed to constant intramuscular drip. For 24 hours, 600,000 units of penicillin were given in this way, and thereafter 960,000 units were given every 14 hours until the medication was discontinued on October 12. The total duration of penicillin therapy was 14 days, and the total amount of penicillin administered was 10,000,000 units. Table 1 presents the details of the therapy and the penicillin

TABLE 1. Method of Administration, Dosage and Serum Concentration of Penicillin in Case 2

DATE	ADMINISTRATION BY HOURLY INTRAMUSCULAR INJECTION			ADMINISTRATION BY INTRAMUSCULAR DRIP	
	DOSE	24-HOUR DOSAGE	SERUM CONCENTRATION	24-HOUR DOSAGE	SERUM CONCENTRATION
	units	units	units per cc	units	units per cc
9/28-9/29	10,000	240,000	0.10		
9/29-9/30	15,000	360,000	0.16		
9/30-10/1	15,000	360,000	0.15		
10/1-10/2	20,000	480,000	0.25		
10/2-10/3	25,000	600,000	0.33		
10/3-10/4	30,000	720,000	0.68		
10/4-10/5	35,000	840,000	0.88		
10/5-10/6	40,000	960,000	0.58		
			0.97		
			1.10		
			0.68	600,000	0.10
10/6-10/7					0.35
					0.50
				960,000	0.69
10/7-10/8					0.91
10/8-10/9				960,000	0.91
10/9-10/10				960,000	0.73
10/10-10/11					0.73
				960,000	0.70
10/11-10/12					

concentrations in the serum of blood collected either 45 minutes after an intramuscular injection or during constant intramuscular administration. Following the discontinuation of penicillin therapy, the patient was kept under observation in the hospital for 10 weeks until discharge on December 24.

Within 48 hours after the initiation of penicillin therapy, the rectal temperature failed to rise above 100°F and thereafter remained within normal limits. There were no further symptoms, and the patient remained entirely free of symptoms. One small, tender, red spot appeared on the tip of the left little finger on October 5, but no evidence of emboli occurred thereafter. The corrected sedimentation rate dropped to 0.39 mm per minute on October 23 or 25 days after the onset of therapy, and subsequently remained well within normal limits. A blood culture on September 29, taken 1 hour after the last previous intramuscular injection of 10,000 units of penicillin, was still positive for *Str. viridans*.

another culture on September 30, taken 1 hour after previous injection of 15,000 units, was likewise positive. The next ten consecutive cultures taken during therapy, however, failed to show streptococci. From the time the therapy was discontinued on October 12 until the time the patient was discharged on December 24, fourteen additional negative cultures were obtained.

Following discharge from the hospital the patient was examined every 1 or 2 months in the Follow-up Clinic. She remained entirely symptom free and, when last seen on October 9, 1946, was leading a normal active life. The radiologic findings remained essentially the same as those described above. Otherwise, physical examination revealed no abnormalities. At all visits the corrected sedimentation rate was well within normal limits and the blood cultures showed no growth. During a total follow-up period of 24 months since discontinuation of therapy, twenty-seven consecutive blood cultures were negative.

DISCUSSION

The clinical backgrounds in these cases were rather similar. Both patients were relatively young women who had developed rheumatic heart disease following a single attack of rheumatic fever early in childhood, both had been observed at the House of the Good Samaritan during the original attacks of rheumatic fever, and both had been examined at intervals thereafter in the clinics of various hospitals. In both cases the valvular lesion was only that of mitral regurgitation, and the heart was of normal size or slightly enlarged. Until the onset of the bacterial infection both patients had been physically active and able to lead normal lives. In neither case could a history be elicited of preceding dental work or respiratory infection.

The clinical course of the bacterial endocarditis, however, was not the same for these patients. The illness in Case 1 began rather suddenly with a chill about two months before admission. From the onset until the effect of penicillin therapy the patient was acutely ill, with a high fever and a rapid heart rate. On admission to the House of the Good Samaritan, she was at times lethargic and at other times delirious. On the other hand, the illness in Case 2 began rather insidiously about four months before admission to the hospital. The patient had persistent symptoms, but at no time did she have a high fever or seem acutely ill. The serum antistreptolysin titers, as might be expected, were low in both cases.

The organisms isolated from both patients were classified as *Str viridans* on the basis of the appearance of their colonies on 5 per cent horse-blood agar plates. Serums for Lancefield grouping were not available in the laboratory at that time, and no other attempts were made to subclassify the strains.

The in vitro behavior of the organisms in the presence of penicillin was of particular interest. The streptococcus isolated in Case 1, in which the patient was acutely ill, was found to be highly susceptible to penicillin. Growth in broth was prevented by as little as 0.02 units per cubic centimeter, and in the presence of concentrations of penicillin slightly in excess of this even a heavy inoculum of the organisms could be completely or nearly completely sterilized within twenty-four hours. In contrast, the

strain isolated in Case 2, in which the patient was mildly ill, was relatively resistant to penicillin. To prevent growth of the bacteria in broth it was necessary to have a concentration of 0.40 units of penicillin per cubic centimeter. Furthermore, the rate at which the organisms were killed even by an excess of penicillin was considerably slower with the strain in Case 2 than with that in Case 1. Thus, when penicillin-sensitivity tests were performed on the strain in the former, sterilization could be completely or nearly completely effected only if a relatively small inoculum was used. If the inoculum contained more than 20,000 organisms per cubic centimeter, sterilization could not be produced by even 100 units of penicillin, and after twenty-four hours of incubation numerous live organisms were still present. Further details and discussion of the in vitro behavior of these strains are included in a report published elsewhere.¹⁵

The patient in Case 1 was cured relatively easily with penicillin in moderate dosage given by intermittent intramuscular injections every three hours. This favorable result is what might have been expected from the knowledge of the high penicillin sensitivity of the causative organism. The persistence of small red spots for a period of sixteen weeks is of interest.

The excellent response of the patient in Case 2 to penicillin is more surprising. Even though she was clinically not acutely ill, the disease had been present for at least four months prior to the initiation of therapy, and as already pointed out, the infection was caused by an organism whose bacteriostatic sensitivity to penicillin was relatively poor in comparison to that of organisms isolated in most cases of subacute bacterial endocarditis. That a cure was actually obtained was probably due, at least in large part, to the fact that a high penicillin concentration in the blood was maintained almost constantly throughout the period of treatment. Concentrations above the bacteriostatic sensitivity level of 0.40 unit were present for most of the time after the first four days, and for a period of five or six days the serum concentration was at a level equal to nearly twice the bacteriostatic sensitivity of the organism.

Another interesting feature in Case 2 was the successful outcome after treatment for only two weeks. Although not necessarily contradictory, this result is particularly worthy of note in view of the opinion recently expressed by Bloomfield and Halpern¹² that penicillin therapy should be continued for at least two months.

There can be no doubt that these 2 cases represent true cures of subacute bacterial endocarditis. The diagnosis was firmly established on both clinical and bacteriologic grounds before therapy was instituted. Both patients had fever and multiple evidences of emboli, as well as repeated and consistently positive blood cultures for *Str viridans*. Both patients responded promptly to therapy. All evidences

of inflammation, including the sedimentation rate, and all embolic phenomena eventually disappeared. Numerous blood cultures during and after treatment continued to be negative. Subsequent to discharge from the hospital the patients were examined every one or two months and were found to be clinically free from disease. Furthermore, the blood sedimentation rates were normal, and the blood cultures were negative at every clinic visit. The total follow-up since discontinuation of the penicillin therapy was twenty-four months for both patients and both were leading completely normal physically active lives.

SUMMARY

Reports are presented of 2 cases in which the patients were cured of subacute bacterial endocarditis by penicillin therapy.

The penicillin resistance of the originally isolated causative organism in one case was greater than that of any other successfully treated case that has been reported in the medical literature.

The correlation of the clinical picture with the penicillin sensitivity of the causative organism is of interest: one patient was extremely ill, and the causative organism was extremely sensitive to penicillin, and the other was mildly ill, and the causative organism was relatively resistant to penicillin.

In one case a cure was obtained after only two weeks of penicillin therapy.

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HEMOSTASIS BY THROMBIN AND FIBRIN FOAM IN SUPRAPUBIC PROSTATECTOMY*

An Analysis of 40 Cases

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BOSTON

THE operative cure of the patient suffering from prostatic obstruction involves three major problems — control of renal function and disordered water balance, control of infection and control of hemorrhage at operation and subsequently.

Dehydration, which is often present in prostatic obstruction, has recently been clearly demonstrated to be responsive to various forms of parenteral fluid therapy based on the chemical determination of the blood electrolytes. A proper acid-base equilibrium of the blood and tissue fluids, which is well recognized as a prerequisite to the successful outcome of any major surgical operation, is especially necessary before prostatectomy. The skillful administration of water, plasma and saline and glucose solutions accordingly plays an important role in successful therapy, the details of this aspect of the treatment of prostatism were presented by Simeone¹ in 1941.

Many of the less severe degrees of urinary infection can be allayed with the aid of a urinary antiseptic such as sulfadiazine. Of equal or greater value is the prevention of infection by avoiding, whenever possible, the use of the indwelling urethral catheter, for the urethra is known to be a constant source of bacteria that rapidly increase in number and virulence owing to the inevitable trauma of an indwelling catheter. Therefore, when drainage of the bladder for longer than a day or two before operation has been necessary, it has been the practice in this clinic to introduce a suprapubic catheter through a trocar or so-called "punch." This procedure causes no discomfort, and the bladder can easily be kept aseptic by the use of a closed system connecting the catheter with the drainage bottle. Austen's² report gives the details of the punch method of bladder drainage.

The most recent advances in prostatic surgery relate to the control of hemorrhage at operation and subsequently. This problem has long been found difficult, and many devices have been applied to its solution. Packing around an indwelling catheter, ligation of bleeding points or coagulation by the high-frequency electric current and, especially in recent times, the pressure exerted by a

distensible rubber bag (Pilcher) have been used with varying degrees of success. The packing and pressure-bag methods, even if efficient in controlling bleeding, almost always cause an extreme degree of vesical discomfort and tenesmus that makes the day or two after operation uncomfortable and requires heavy sedation. The electrocoagulation or actual ligation of bleeding vessels frequently fails to bring about really adequate hemostasis, because the actual bleeding points deep in the prostatic cavity are difficult to reach and identify.

The use of a coagulant that is normally a factor in the production of a blood clot — namely, thrombin — remains to be explored. Its action in converting soluble fibrinogen into insoluble fibrin can be considered the fundamental reaction in the coagulation of the blood.³ Until recently, however, thrombin was difficult to isolate in a sufficiently concentrated form to be of value in producing a firm and adherent clot over a bleeding surface. Also, it is evident that some sort of matrix by which the thrombin can be prevented from being washed off in the blood stream is needed. Such a supporting substance has been found in fibrin in a form with many spongelike interstices that is called, for convenience, "fibrin foam."⁴ Both thrombin and fibrin foam are but two of the many important results of the work of Cohn and his colleagues⁵ in the Department of Physical Chemistry, Harvard Medical School, under contract between the Office of Scientific Research and Development and Harvard University, to study the fractionation products of human blood plasma. Without doubt the most exacting circumstances demanding hemostasis are those encountered in neurosurgery. In this field the investigations of Bailey and Ingraham⁶ have shown the great value of the fibrin-foam method, in which the foam remains permanently in the tissues but is quite nonirritating and rather quickly absorbed.

The observations presented below, in which the foam method is applied to the prostatic cavity, do not concern the factors of absorption of the matrix. As a matter of fact, the foam has been found to be insoluble in urine.

METHOD

The solution of thrombin is made by dissolving the dry powder in about 10 cc. of an isotonic solu-

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tion of sodium chloride. In this solution pieces of foam about 1.5 to 2.0 cm square are immersed and agitated until the air in the interstices is largely replaced by fluid. These pieces are then placed in the cavity of the prostate so as to fill it entirely, beginning at its apex and continuing to include the torn edge of the trigone (Fig. 1). Pressure is exerted over

possible, sparking by the high-frequency electric current should be employed. When such a rare arterial spurter is present, it is usually situated just under the torn edge of the trigone in an area readily accessible without removal of any of the foam already in place. Since occlusion of vessels by sparking, even though light, is accompanied by tissue

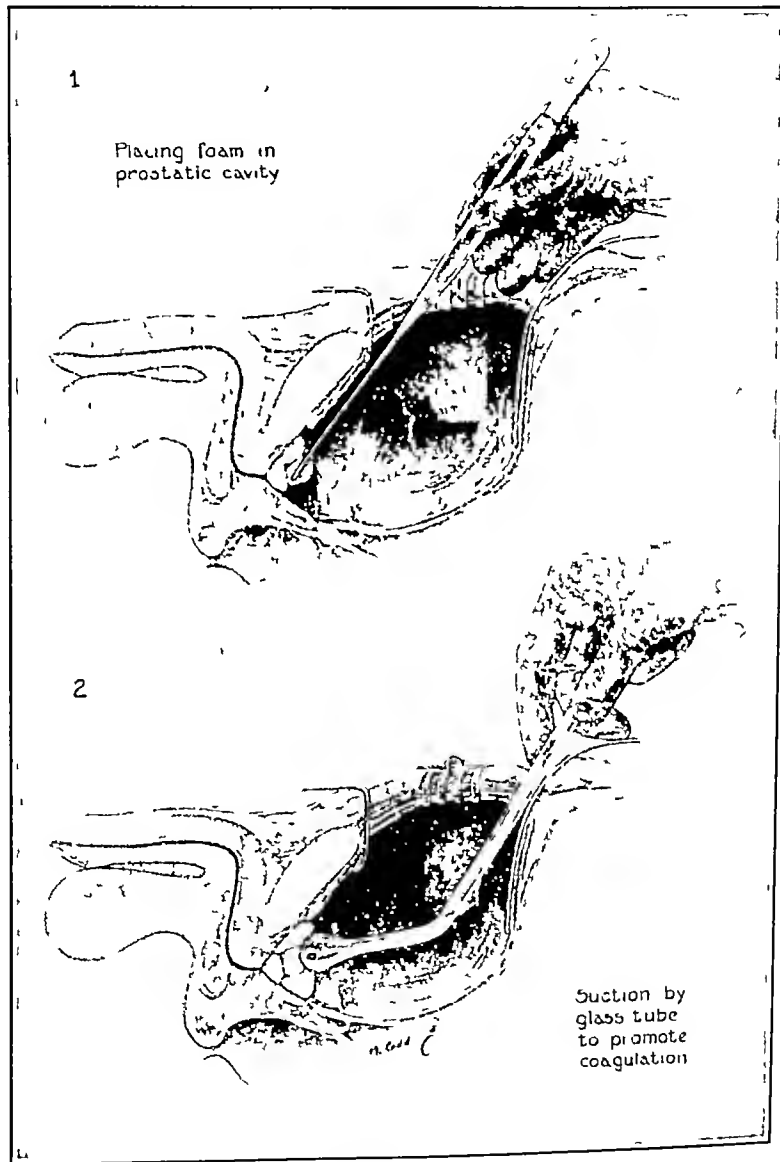


FIGURE 1

the mass of foam by a thin layer of surgical gauze, and the whole area is subjected to suction through a bent glass tube in the form of the usual perforated douche nozzle. Since the blood is thus drawn into the thrombin-soaked foam, coagulation takes place in about five minutes. Usually no additional hemostatic measure is needed. If a single vessel bleeds so sharply that control by foam and pressure is not

necrosis, this method should be used only when unavoidable.

Patience, continued pressure and suction are the essential factors in the production of hemostasis by this procedure. After complete hemostasis has been obtained the bladder is closed by interrupted sutures of fine catgut. A catheter with a mushroom end (Pezzer), of a size approximately No. 20 Fr., is ad-

sted in the upper angle of the wound for drainage of urine. The structures in front of the bladder are sutured by sutures of fine silk. After operation lavage of the bladder is avoided entirely, indeed, in the absence of bleeding and clot formation such irrigation has no place. The siphon effect of the suprapubic tube is sufficient to carry away the urine soon after it reaches the bladder from the kidneys. A "quiet" bladder, with no stimulus either to expand or to contract, results. This is a significant factor in prompt healing and a smooth early convalescence.

Following operation, fluids are forced to at least 1000 cc daily. The patient is urged to get out of bed on the first postoperative day for a short period in both morning and afternoon. The suprapubic catheter is allowed to remain in place until about the third or fourth day, when the urine is again cleared by the oblique route of insertion, abdominal pressure quickly closes the sinus tract after removal of the catheter, and spontaneous urination is resumed a day or two later. The foam is passed from the bladder in the form of small, slimy bits, without any suggestion of obstruction. If spontaneous urination seems delayed because of the foam, the single gentle passage of either a metal catheter or a sound serves to dislodge the foam. This passage, however, is rarely needed.

RESULTS

In the most recent 88 consecutive cases of prostatic obstruction at the Peter Bent Brigham Hospital, 36 patients were treated by transurethral and 12 by perineal prostatectomy, the suprapubic route was employed in 40 cases, fibrin foam being used as a hemostatic agent.

The age of this last group of patients was as follows: fifty to sixty years, 8 cases; sixty to seventy years, 22 cases; and seventy to eighty years, 10 cases.

The smallest prostate gland weighed 20 gm, and the largest 107 gm, the average being 40 gm.

Preoperative drainage of the bladder was effected through a suprapubic punch in 6 cases and through a urethral catheter (for a short period) in 7, no preoperative drainage was performed in 27 cases.

The urine was clear on inspection two to four days after operation. The suprapubic drain was removed, on the average, slightly over five days after operation. The wound was healed and dry and voluntary urination had been resumed, on the average, eleven and a half days after operation. The reduction in the length of time from operation to resumption of voluntary urination — from fourteen and a half days in the first 10 cases to nine and a half days in the last 20 cases — is to be explained by increased experience regarding the interval after which bladder drainage could safely be abandoned.

Especially noteworthy is the fact that in no case was there any secondary bleeding. Lavage of the bladder was early abandoned, and the distinct impression was obtained that a bladder thus put at

rest, without stimulus to its normal action of expansion and contraction, is an important factor in early healing of the injured area.

SUMMARY

The method employed in the use of fibrin foam as a hemostatic agent after suprapubic prostatectomy is discussed, and the results obtained in 40 consecutive cases are described.

Since the above clinical observations were made, operations have been performed in several additional cases in which bovine thrombin in a matrix of gelatin (Gelfoam) was used instead of the human products. Hemostasis by these materials seemed as satisfactory as that produced by human fibrin and thrombin.

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DISCUSSION

DR JOHN M. FALLON (Worcester). I am not competent to discuss Dr. Quinby's paper, but it has been suggested that I talk to you about the use of fibrin foam in general surgery, because these new fractions are, in my opinion, as important in clinical surgery as the older fraction — plasma — to which we are more accustomed.

Human blood fractions, supplied to the clinic through the kindness of Dr. Francis Ingraham by the Department of Physical Chemistry, Harvard Medical School, have been used one hundred and seventy-five times in 160 cases in general surgery. The fractions were thrombin, fibrin foam and Fraction I (fibrinogen), and the purpose of study was the development of applications in general surgery. I shall discuss only the combination of fibrin foam and thrombin that Dr. Quinby has described.

First, so far as the hemostasis of incisions into solid organs is concerned, the most useful application has been in thyroidectomy. Only the larger spurs need be clamped, with six to ten clamps on each lobe. These clamps are tied, and no second round of clamps is applied. The remnant of the thyroid gland is not sutured. Sheets of foam on the cut surface do the rest. The advantage consists not only in reduction of suture material but also in avoidance of trauma to the thyroid remnant. One may intend to leave a fifth or a sixth of the gland, but if such a fifth or sixth is full of sutures it may be physiologically a tenth. The suture that the foam supplants endangers the recurrent nerve crossing behind the gland. Foam has also successfully controlled oozing from incisions into the pancreas, liver and kidney.

Secondly, to obtain hemostasis on soft surfaces and in areolar spaces — spaces on which it is difficult to apply clamps, foam invariably succeeds. An especially rewarding application is to tissues distorted by disease and situated near vulnerable structures like the ureter, phrenic nerve and twelfth nerve, when the foam is substituted for blind clamping and deep sutures. The most frequent application in this group is to the subvesical veins, which are encountered in hysterectomy and in vaginal operations. The neck, the erectile tissues of the labia, the retroperitoneal spaces, the mesentery and the intestine are good examples of such soft areas.

Thirdly, control of direct hemorrhage of large vessels, which was attempted merely to show that it should not be

done, was not tried in human subjects. In eight operations on dogs, major arteries up to 4 mm. in diameter were either opened on the side or transected. With normal blood pressure, the arteries of 2 mm. and sometimes those of 3 mm. were controlled by foam and pressure. Some clots blew off when the blood pressure was artificially raised, but after the blood pressure had returned to normal, new applications of foam invariably held. Two arteries of 4 mm. could not be controlled by foam until the pressure had fallen to dangerous levels.

The use of foam is not recommended for openings into major vessels. In arteries there is the hazard of a large hydraulic pressure acting over a large area, and in veins the added risk of insucked thrombin, causing thrombosis elsewhere in the body. One of my colleagues, however, suddenly faced with a laceration of the vena cava in a patient in bad condition, successfully held a pad of foam over the opening by suturing peritoneum over it. This patient ultimately died from other causes, and autopsy showed neither hemorrhage in the area of the vena cava nor thrombosis elsewhere.

Fourthly, foam is employed as a filler of cavities. Foam is a stuffing that has hemostatic qualities and can be replaced by reparative tissues. Usually only a small amount is needed. Up to 25 cc. has been used, however, without visible ill effect. A dramatic application has been in the removal of Bartholin's cysts. Often the small artery at the upper end of the cyst escapes the clamps, retreats into the spongy paravaginal tissues and bleeds. Foam has ended all this. Wens, stripped varices and ganglions—that is, areas that can later be watched from the surface—when filled with foam have done well. And deeper, larger areas that cannot be watched, like the pararectal space, seem to have done well.

Fifthly, foam is used as a dressing. Following an accidental observation that better epithelium seemed to grow more quickly under foam, such dressings were used on several skin

defects and in two defects of the mucosa (mouth and es-moid), with good results. Foam, incidentally, is an excellent dressing for anal operations. At the end of an operation the anoscope can be reinserted to check what has been done without fear of stirring up hemorrhage if followed by a foam plug. Foam has also been used as an internal dressing, wrapped around intestinal anastomoses in dogs and in human beings, but it is not yet possible to report the results.

Complications include the danger of squeezing thrombus into a large vein. Two out of 160 patients had femoral thrombosis. This incidence is high, but the total group is small for conclusions. However unscientific it sounds, this was a group of patients picked from a larger total and containing most of those members of the total who were likely to have thrombosis.

Finally, blood fractions are neither an excuse for carelessness nor a substitute for good judgment, but the knowledge that blood fractions were available led me to attempt procedures that a few months previously would not have been considered. Amusingly, the fact that the foam was available has increased my respect for simple pressure. Often, by the time the foam reached the table, the bleeding had stopped, when foam was added, however, there was no fear that hemorrhage would occur.

DR. FRANC D. INGRAHAM (Boston): There is nothing for me to add to Doctor Quinby's paper or to Doctor Fallon's discussion. My experience has been chiefly with the use of the materials described in neurosurgical patients.

I should like to emphasize the facts that during the war all these materials were derived from Red Cross blood and that none of them were distributed to civilians except as testers for the armed forces. After the material had been released by the testing group, it was sent to the Army or the Navy.

TREATMENT OF MENTAL ILLNESS AT HOME BY SMALL DOSES OF INSULIN

An Appraisal of Results in Twelve Cases

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SINCE the introduction of insulin coma in the treatment of certain mental disorders by Manfred Sakel in 1933, the method has gained wide acceptance. The most extensive evaluation of the results with insulin coma is contained in a recent report of the New York Temporary Commission on State Hospital Problems,¹ which strongly favors insulin as being of definite value in the treatment of schizophrenia. This report is based on 1128 patients treated with insulin and on 876 control patients who did not receive any form of shock treatment. The former group had a definitely shorter period of hospitalization than the latter, as well as a longer period of satisfactory adjustment at home and a higher level of usefulness in the community. This type of therapy is drastic, however, and requires hospitalization, and there are a large group of patients whose mental condition does not require hospitalization. The purpose of this paper is to present experiences with a modified form of insulin-coma therapy in such patients at home.

The possibilities of insulin subcoma as a method of therapy have been only scantily explored. The

first report of the therapeutic use of mild hypoglycemic shock was that of Cowie et al.,² who in 1923 noted that depressed states frequently cleared up during the insulin treatment of diabetes.

Subsequently, other reports suggested that such therapy might be beneficial. Among these is the work of Targowla and Lamache,³ who in 1926 used insulin on 2 undernourished, depressed psychotic patients, and of Miskolczy,⁴ who in 1927 worked with insulin in a variety of neurologic conditions.

In 1929 Appel and his associates⁵ found insulin subcoma of value in improving the appetite and the nutritional and mental status of patients suffering from neurasthenia, depressive states and dementia praecox. The amount of food intake was increased in practically all cases, and the gastrointestinal function seemed to be improved. The dry, gray, flabby skin soon took on a healthy appearance. Not a few patients gained weight to an extent not previously experienced—a remarkable observation, since most of the patients were over forty-five years of age.

The first report on the prolonged therapeutic use of repeated mild hypoglycemic shocks over a long period in mental disorders was that of Polatin, Spotnitz and Wiesel⁶ in 1940. Their group included

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3 patients with schizophrenia, manic-depressive psychosis and psychoneurosis and 4 with psychoses due to brain damage. The treatment consisted of daily hypodermic injections of small doses of insulin — initially 5 units, increased by 5 units daily to the point of mild hypoglycemia. The hypoglycemic symptoms usually began to manifest themselves about two hours after injection and gradually increased in severity. Patients remained in this state for from fifteen to forty-five minutes, depending on the degree of the hypoglycemia, which usually terminated with breakfast three or four hours after injection. During the hypoglycemia, the patients were up and about and were able to feed themselves at breakfast without assistance. They were treated daily for an indefinite period until improvement occurred. This ranged from one week to eighteen months. It was noted that most patients gained weight and that all became easier nursing and feeding problems. Of the 22 patients treated, 1 recovered, 12 were improved, 5 were slightly improved and 4 remained unimproved. No coma, allergic manifestations, convulsions or injuries occurred. These studies indicate that mild hypoglycemic shock is of considerable value in the treatment of mental disorders. The authors emphasize the fact that beneficial effects were slowly accumulative and that prolonged treatment was necessary before satisfactory results were observed. Subsequent reports of these authors^{7, 8} in a large series of cases have confirmed their original impressions.

In 1940 Bennett and Miller⁹ tried subshock doses of insulin in psychotic patients presenting difficulties in management. The treatment was given in 125 cases presenting extreme nursing problems, and in nearly every case of acute manic excitement was controlled without sedatives within an average period of thirty-six hours after adequate insulin dosage. The use of sedatives was practically eliminated in cases of extreme psychomotor activity.

Ambulatory insulin therapy was utilized by Tomlinson and Ozarin¹⁰ in 1942, according to the method described by Polatin and his co-workers. In a group of 52 unselected cases, 34 patients (65 per cent) improved, 5 (10 per cent) improved and then relapsed and 13 (25 per cent) showed no improvement. A year after this program had been initiated, 13 patients (25 per cent) had been paroled from the hospital. In dementia praecox, paranoid type, which comprised the largest number of cases treated, 60 per cent of patients were definitely improved. It is interesting that a patient with Alzheimer's disease improved and that 2 parietic patients showed a favorable response.

Rennie,¹¹ in 1943, reported 28 heterogeneous cases in which insulin in doses of 50 to 90 units daily over a period of twenty to fifty days gave especially gratifying results in the relief of excitement, overactivity, inner tension and, particularly, anxiety. Rennie found that insulin sedation was superior to

sedation by ordinary chemical methods, the effects being more incisive and lasting. It was apparent that dramatic relief could be achieved with insulin in various kinds of excitement whenever anxiety prevailed. Insulin therapy permitted a marked degree of relaxation, released ability to discuss pre-occupations easily and provided the therapist with a real opportunity to understand the patient and his basic needs.

Beneficial results with subcoma insulin have been reported in the treatment of acute alcoholism¹² and the relief of severe migrainous headaches¹³ and as an aid in rehabilitating soldiers suffering from acute panic, protracted states of anxiety and chronic weight loss.^{14, 15}

A recent report by Sands,⁶ summarizing his experiences in 163 cases, advocated subcoma insulin in the treatment of war neuroses.

Referring to insulin subcoma treatment of ambulatory patients, Brickner¹⁷ states that the method is extremely useful in the relief of tension associated with practically every type of mental or emotional disturbance.

The following report deals with the results of prolonged subcoma insulin treatment in a consecutive series of 12 ambulatory patients with chronic mental illness that had been refractory to other forms of management.

METHOD

Breakfast is withheld each morning. Insulin injections are given six times a week in increasing amounts until mild hypoglycemic shock, manifested by weakness, copious perspiration, hunger and drowsiness, is produced. Usually 50 to 90 units is a sufficient dosage. When mild hypoglycemic shock occurs, the dosage is maintained at the same level so long as the optimum effect continues. In some cases, however, the dosage must be further increased.

Mild coma occasionally supervenes, but the patient is deliberately prevented from going into deep coma. Generally it is observed that after several weeks of continued insulin therapy, the patient develops a certain amount of sensitivity to insulin, and thereafter it is possible to obtain reactions with a reduced dosage. The insulin dosage is at all times kept at a minimal level, and the intensity of the hypoglycemia is controlled by feeding. In this way, patients feel more comfortable, whereas with larger doses they are apt to express feelings of discomfort and even to suffer from nausea and other gastrointestinal manifestations.

As a rule the hypoglycemic manifestations appear in approximately an hour. If insulin is injected intravenously the symptoms usually appear in an appreciably shorter period. Generally the patient is quite comfortable during the first half hour, although there are individual variations.

Experience shows that frequent modifications and variations are often essential for the success of this

method During the treatment patients are up and about, but, if they prefer to lie down when the hypoglycemic manifestations become upsetting, they are permitted to do so

It is advisable that the patient be kept under constant observation by the physician or a trained nurse, and that the pulse, blood pressure, respiration and general clinical status be checked at frequent intervals Those in attendance are instructed regarding the complications that may arise and their management Barbiturates are contraindicated during the insulin series, since they may negate the effect of the insulin

The patient is permitted to remain in a state of mild hypoglycemic shock for a variable length of time, and termination is then brought about as described above In the early phases of hypoglycemia, psychotherapeutic discussions are carried out

The results of the method of therapy in the following 12 cases appear to justify its continued use

CASE 1 A 28-year-old married Italian immigrant who had suffered considerable early privation in his native land came to America at the age of 17 and successfully operated a barber shop until November, 1943, when in response to wartime stress he developed marked tension, restlessness, anxiety and obsessive fears, the most prominent among which was worry that he would slit the throat of his customers while shaving them This led to a marked inefficiency and almost complete incapacity in his work He complained of weakness, pain, dizziness, insomnia, anorexia, tremors and temper outbursts

Insulin subshock was begun on January 28, 1945 Improvement was first noted on February 26, and thereafter there was a gradual abatement of all symptoms until complete recovery on May 13

The patient was entirely well at follow-up examination 8 months later

CASE 2 A 30-year-old married Italian woman with a history of attacks of depression at the ages of 16 and 26, succumbed to a third depressive psychosis in March, 1944, following her husband's entry into the armed forces

The symptoms consisted of insomnia, numerous somatic complaints, worry, fatigue, spells of weeping and obsessive longing for her husband The illness continued for a year, and the patient lost a total of 39 pounds in weight

She made a suicidal attempt by swallowing iodine Neither hospitalization nor electric shock treatments were permitted The constant threat of suicide made the situation desperate

On March 17, 1945, insulin subcoma treatment was begun, and the patient made a dramatic improvement in 5 weeks In 12 weeks she had regained 23 pounds in weight. She was cheerful, interested, self-reliant and confident about the future Recovery persisted

CASE 3 A 40-year-old married woman, whose family history revealed suicide of one parent and whose early life had been essentially normal, first developed symptoms in 1941 following an attack of influenza She showed the typical reactions of a shut-in personality Tension, nervousness and obsessive fears persisted for months, resulting in marked incapacity There was a sense of impending disaster, as well as various somatic complaints Extreme emotional instability — characterized by laughing and crying spells, agitation and panic reactions — resulted in a state of utter helplessness This condition remained unabated except for short periods of relief during the summer months

Prolonged treatment with barbiturates and other drugs was unsuccessful Orthodox psychotherapy by several competent psychiatrists, as well as several years of psychoanalysis, was of no avail in alleviating the symptoms Electric-shock therapy was equally unsuccessful, except for a brief period of partial relief of symptoms An exhaustive medical examination failed to reveal any evidence of organic disease

In May, 1945, insulin therapy was initiated, beginning with a dose of 10 units and increasing the dosage daily until symptoms of mild hypoglycemic shock were present Sixty treatments in all were given, the maximum dose being 90 units

After 5 weeks of treatment, there was a gradual and remarkable remission of the symptoms Tension and anxiety diminished, the weight increased steadily and the patient was able to resume social activities and derived considerable pleasure and satisfaction out of life She became more accessible to psychotherapy, and improvement continued steadily until complete recovery 10 weeks after the initiation of the therapy

The patient subsequently remained well, and for the first time in 5 years was not confined to bed during the winter

CASE 4 A 56-year-old married man with a noncontributory family history had suffered for 6 years from pain in the post-thoracic region radiating laterally A diagnosis could not be established despite the concerted efforts of many specialists Novocain nerve-root injections were given, but after 3 weeks of comparative comfort the pain returned

The patient suffered for 8 months, during which x-ray treatment of the spine gave temporary relief Exercises and diathermy given by an osteopath aggravated the pain Opium gave partial amelioration during hospitalization After a second novocain injection the patient collapsed completely and had to remain in bed for several days

A depression followed The symptoms consisted of despondency, loss of weight and poor appetite No response was obtained to sedatives

At a private sanatorium a course of electric shock treatments brought some palliation for 9 months, but in February, 1945, the patient relapsed into depression Various forms of medical management proved ineffective The patient had crying spells and suffered from anhedonia, insomnia, inability to concentrate, a host of bodily symptoms and extreme anxiety

Insulin subshock treatment was begun on May 11 The response was most encouraging, the patient began to gain weight, the appetite improved and he was able to work and showed renewed and sustained interest He was treated until August 27, when he felt well enough to take a vacation for a week Improvement lasted until October 9, when the patient reacted to slight external stress by becoming mildly depressed

He continued to receive additional treatment intermittently, during which his condition fluctuated For an occasional day or so he slept poorly and complained of headaches and vague pains In general, however, his condition remained satisfactory He was able to attend to his business duties, which he had not been able to do satisfactorily before treatment The depression largely abated, and the patient gained weight and appeared well

CASE 5 A 37-year-old, overprotected, married Italian woman, with a history of nervousness in childhood and difficulty in adjustment in play life, first succumbed to a clearly defined illness in the post-partum period of her first delivery She developed weakness, apathy, loneliness and seclusiveness Two years previously, following the death of her mother, she had been depressed for 4 months

In June, 1945, she suffered an acute turmoil reaction characterized by irritability, mood swings, agitation, delusions and hallucinations No effect was obtained by a variety of medication or by a change of environment

Insulin subshock treatment was immediately begun, and in 2 weeks the symptoms began to clear A total of 92 subshock treatments were necessary to restore the patient to mental health

She was well when last seen

CASE 6 A 26-year-old married man had been insecure, inadequate, emotionally unstable, suspicious and distrustful since the loss of his parents at an early age He constantly complained of somatic disease, lack of energy and fatigue and indulged in self-reproach His mood was chronically depressed

Insulin subshock treatment was begun on June 30, 1945, and in a month the patient was able to handle his anxiety more adequately His emotional life reached an even keel and his outbursts became infrequent Treatment was continued with some interruptions until September 15 The pa-

ent was considerably improved but not completely relaxed further treatment was omitted, however

The patient was mentally recovered at follow-up examination 6 months later

CASE 7 A 42-year-old spinster became seriously ill in 1931 following a clandestine affair with a married man interested only in exploiting her. Suffering from anorexia and vomiting, he gave up her job and retired to a life of invalidism. She radically sank into a state of tiredness, lassitude, self-depreciation, seclusiveness and emotional instability. Regurgitation and vomiting followed any suggestion of social intercourse.

Despite numerous attempts at medical management and psychotherapy, the condition continued unabated for 14 years—the only significant change being that the patient became more depressed and despondent. Since the family refused permission for electric-shock treatment and frowned on hospitalization, insulin subcoma treatment at home was begun on July 18, 1945, and continued for 4½ months.

The first short period of improvement was noted in 6 weeks thereafter, intervals of well-being became more prolonged. Psychotherapeutic sessions were soon possible with a patient who had previously been inaccessible. Hope and confidence came into the life of a woman who had been mentally ill for 14 years. The patient returned to work, and social adjustment was excellent.

CASE 8 A 40-year-old married woman, whose mother had been neurotic and whose father had been alcoholic, had led a gay, cheerful and useful life until a cesarean section in 1942 resulted in a dead infant. Both the patient and her husband were deeply grieved over the loss, with intensification of dissatisfaction and yearning when future months left them barren and childless. The patient began to blame herself and expressed feelings of guilt over past sexual indiscretions and excessive concern over a brother's neuropathic tendencies. This condition continued intermittently until 1943, when she became seriously depressed and was treated with electric shock, which gave only temporary relief.

In June, 1945, the patient presented a picture of anxiety, somatic disturbances, marked phobias and a fear of death oscillating with periods of gaiety and euphoria. Insulin subcoma treatment was begun in August, and continued for 4 months, the patient receiving a total of ninety-six treatments. Ten weeks of treatment resulted in loss of anxiety and of feelings of guilt. She gradually became more objective, contented, active and stable in her adjustment to her environment.

Follow-up study 4 months later revealed that the patient had not lost any of the gains made under insulin subcoma treatment.

CASE 9 A 46-year-old, married, artistic woman, overwhelmed by the shock of several deaths in her family and a serious heart ailment in her husband, succumbed in 1944 to an illness marked by fatigue, anxiety, gastric distress and abhorrence for food and water. Financial difficulties, more bereavements and an increasing feeling of loneliness seemed insuperable obstacles to recovery. Of psychological interest was the fact that on several occasions news of a death in the family came at the time the patient was eating a meal, avoidance of food and drink was the result of this conditioning. Amenorrhea of 6 months' duration developed, the patient took to barbiturates, with indulgence to levels of mild toxicity.

Insulin subshock treatment was begun on August 21, 1945. Improvement was noted in 1 month, the patient slept well without medication and actually experienced pleasurable sensations of hunger and thirst without distress at their satisfaction. At the end of fifty treatments she had gained 12 pounds in weight. Curiously, she showed little enthusiasm for her recovery and weight gain and a reluctance to continue with the therapy, which was soon discontinued.

Follow-up after 5 months revealed that patient had slipped slightly and returned to her former weight level, but as she was no longer a barbiturate addict, she could engage with interest and enjoyment in art, and seems to have partially maintained her improvement.

CASE 10 A 47-year-old married man became ill in 1942, when he suspected his wife of a clandestine love affair. The symptoms consisted of insomnia, worry, crying spells, in-

ability to concentrate, loss of interest and spontaneity. He hired detectives to trail his wife and contemplated divorce. In May, 1944, he had an attack of coronary thrombosis. This preyed on his mind and added to the already heavy strain. He constantly chided his wife for his mental state and cardiac disease. During a vacation trip to Florida he was unable to eat or sleep and paced the floor at night, repeatedly accusing his wife, with resulting tension, discord, unrest and bitterness. The distress was not relieved by barbiturates, health resorts, osteopathic treatments and therapy from competent internists and psychiatrists.

Insulin subshock treatment was begun in October, 1945, after assurance by medical specialists that the patient was a good risk. On November 19, a definite upturn was noted. He lost considerable anxiety and gradually became more amenable to psychotherapy. He was able to see his mental problem in a new light.

The remission lasted until February, 1946, when the patient was again beset by doubts, fears and obsessions, which were of short duration, however. As treatment was continued his anxiety completely disappeared, he became jovial and interested in life and resumed the operation of a large and successful business. A total of one hundred and two subshock treatments completed the series.

The excellent home and business adjustment continued.

CASE 11 Following a series of abdominal operations and a loss of 30 pounds in weight, a 38-year-old married woman, whose personality was characterized by egocentricity, selfishness and excessive self-esteem, became embarrassed and self-conscious, lacked interest, ambition and spontaneity and showed excessive irritability when crossed. She complained of fatigue and headaches. The patient took refuge in barbiturates and suffered from mild barbiturate addiction.

Insulin subcoma treatment was begun in November, 1945, and definite improvement was experienced starting with the eighth treatment. Progressively there was a return of appetite and sense of well-being and a gain of 12 pounds in weight. The patient was more relaxed and showed no anxiety or irritability.

After the forty-sixth treatment insulin subcoma was omitted because of a death in the family. Thereafter the patient refused to co-operate for further treatment, stating that the therapy was too restraining and interfered with her social life.

Loss of weight, insomnia, return of irritability and barbiturate addiction followed the cessation of treatment.

CASE 12 The whole life pattern of a 23-year-old man had been characterized by marked inadequacy, self-consciousness, immaturity, lack of drive, initiative or sustained interest, and excessive sensitivity to criticism and rebuke. He broke down in 1939 following the loss of a Government job and consequent severe disappointment in his future. He became more dependent and resentful of others and displayed outbursts of temper. In 1945, examination revealed an introverted, weak-looking man, who was lacking in confidence and complained of poor appetite and insomnia. He had been socially maladjusted, with low spirits, had had frequent crying spells and had not evinced the slightest interest in girls.

Following one interview, conducted under sodium amytal, insulin subcoma treatment was begun in December, 1945. A slight improvement was noted 5 weeks later. The patient gained 10 pounds but was still shaky, unstable and resentful toward his parents. Improvement with further treatment was steadily progressive. Ten weeks after treatment was begun the patient was eating and sleeping well and had gained confidence and poise, and his spirits had risen.

Insulin subcoma treatment has proved valuable in a variety of mental conditions and in many cases that have been refractory to other methods of management.

This treatment has the following advantages: it can be administered in the patient's home and thus obviates the stigma (in the minds of the patient and his relatives) of hospitalization—none of the current drastic methods (electric-shock treatment, insulin-shock treatment and lobotomy)

can be applied readily at home, the method is relatively safe when administered by well trained personnel who are in constant attendance during the period of treatment, the aftercare is rather simple and imposes no undue hardship on either the patient or those in attendance, insulin subcoma is less drastic than actual shock treatment and in all probability produces no irreversible brain damage (patients given as many as one hundred and two subcoma treatments showed no evidence of mental deterioration), the treatment, which is not incapacitating and during which the patient is more or less conscious and usually able to be up and about, has two important advantages over other methods — first, the patient can participate in the psychotherapy, can speak freely of his preoccupations and experiences and can better unburden himself of his distressing thoughts, enabling the therapist to obtain a closer understanding of the patient and his basic needs, and secondly, at the termination of the treatment, the patient is alert and able to join in activities immediately and is not in the toxic, beclouded state characteristic of electric-shock treatment, insulin-coma treatment or heavy barbiturate medication, insulin subcoma greatly relieves basic anxiety — according to Rennie¹¹ the improvement appears to run parallel with the disappearance of dynamic anxiety, although the period of treatment is more prolonged than that in the more drastic types of therapy, the beneficial effects are usually quickly apparent and cumulative, and finally, the effects of subcoma insulin treatment are more incisive and lasting than those with chemical sedation,¹² which often increases anxiety rather than relieving it.

Chemical methods (interviews conducted under sodium amytal) are apt to be rejected by the patient as an aggressive attempt to elicit painful memories that he would prefer to remain hidden.

The period of follow-up study in the cases reported above varied between four and nine months. The final evaluation of this method of therapy must await a longer study of all these cases, as well as a careful investigation of a larger series of cases. The results, however, even in the short period of observation, were quite encouraging and support the findings of Rennie, Brickner, Polatin and others.

Subcoma insulin treatment seems to have almost a specific effect in relieving anxiety and tension. The role that anxiety and tension plays in misinterpretations, delusions and depressions can hardly be overestimated.

A natural disadvantage of this type of treatment in the patient's home is the time factor, several hours of the physician's attention usually being re-

quired. With this precaution, the treatment is relatively safe. It is emphasized that insulin subshock treatment must not be given promiscuously and haphazardly.

SUMMARY

Subcoma (mild hypoglycemic) shock therapy can be administered at home to ambulatory patients with comparative safety. Twelve cases are reported, with results that appear to justify further use of the treatment. The method of administration and the necessary precautions to safeguard the patient are described.

The advantages of repeated subcoma insulin shock treatment are enumerated. Weight gain and increased sense of well-being are important concomitants.

Patients with varying neuropsychiatric conditions, some of which were refractory to other methods of management, showed dramatic improvement or recovery. The beclouded, toxic state regularly encountered with the more drastic types of therapy, such as electric shock and insulin coma, is largely eliminated.

In view of the favorable results encountered and the hopeful reports in the literature, further use of this method is believed to be warranted.

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THE SIGNIFICANCE OF MEDIASTINAL EMPHYSEMA*

A Report of Two Cases

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SPONTANEOUS mediastinal emphysema is now a well recognized clinical entity to which considerable attention has been called. Although Jamman¹ enumerated several routes by which air reaches the mediastinum, the finding of extensive mediastinal and subcutaneous emphysema may at times be too readily attributed to this relatively benign disorder and a serious underlying disease overlooked. It is the purpose of this paper to call attention to that possibility by presenting 2 cases. In Case 1 spontaneous mediastinal emphysema occurred twice, and at the time of recurrence mediastinal decompression became necessary. In Case 2 extensive mediastinal and subcutaneous emphysema was dependent on a serious underlying disorder, discovered at autopsy to be spontaneous rupture of the esophagus. Some points of similarity and the differential diagnosis of the two conditions are discussed below.

CASE 1 I B, a 19-year-old girl, entered the hospital because of severe substernal pain and dyspnea. She had been well until 3 days before entry, when she had noted a head cold. Eight hours before admission she suddenly began to cough and vomited. She felt ill and went to bed, where 15 minutes later she experienced a sudden violent pain over the xiphoid process radiating through to the back but not to the shoulders or arms. The pain was accompanied by severe dyspnea and orthopnea and was aggravated by coughing, by deep breathing, and by lying on the right side. The pain continued undiminished until the time of entry.

Physical examination revealed a well developed, well nourished girl who appeared to be acutely ill and in respiratory distress and who was breathing shallowly and regularly. The temperature was 100.2°F, the pulse 108, and the respirations 30. The blood pressure was 130/95, falling to 110/70 about 4 hours later. Creptus was felt over the face, the occiput, the entire neck and the upper anterior chest. The trachea was deviated slightly to the right. The left side of the chest was hyperresonant, with diminished breath sounds. The area of cardiac dullness was obliterated. The heart sounds were distant, no abnormal sounds were heard. Percussion over the liver revealed dullness. There was no cyanosis or venous engorgement. The remainder of the examination was not remarkable.

The urine was normal. Examination of the blood revealed a hemoglobin content of 80 per cent, and a white-cell count of 14,000, which fell to 6350 on the 2nd hospital day. A blood Hinton test was negative, and a blood culture yielded no growth. A chest roentgenogram, showing a fine line of decreased density to the left of the sternal border that extended down the sternal border and about the pericardium, was regarded as consistent with mediastinal emphysema; there was no pneumothorax. An electrocardiogram was within normal limits.

The patient was placed in bed and given intranasal oxygen, a tight chest binder, codeine and aspirin and sulfamerazine.

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She was fairly comfortable, showing gradual symptomatic and objective improvement, but continuing to run a slight temperature. On the 2nd hospital day muffled crackling or crunching sounds synchronous with systole were heard over the apex of the heart, disappearing within a few hours.

On the 4th hospital day, while the patient was lying quietly in bed and not coughing, she had a sudden recurrence of severe pain and shortly became cyanotic, dyspneic and irrational. Bilateral subconjunctival hemorrhages appeared. Morphine did not control the pain, and oxygen administered with the aid of a Boothby mask gave no relief. The respirations rose to 40, the pulse to 140, and the blood pressure to 160/120. Creptus reappeared over the face, but auscultation of the heart and lungs revealed no abnormality.

The patient was transferred to the operating room, where a 7.6 cm., low-collar incision just above the sternal notch was made under local anesthesia. The muscles were separated in the midline, and a finger was inserted into the superior mediastinum through the suprasternal notch. There was an egress of air, and rapid improvement in the status of the patient followed. The subcutaneous emphysema disappeared gradually, and convalescence was uneventful.

CASE 2 C M, a 58-year-old married man, entered the hospital complaining of abdominal and chest pain of 6 hours' duration. He had consumed considerable quantities of alcohol daily for many years, but he had remained well until 6 hours before hospital admission, when, shortly after carrying a heavy load of brass, he suddenly vomited copious amounts of brown liquid material, there had been no previous nausea. He continued to retch for 5 minutes. He noted marked weakness and shortness of breath, and experienced a severe pain in the anterior and posterior chest and in the upper abdomen, the pain was made worse by deep breathing. After going to bed the patient felt less dyspneic but observed that he was hoarse. Thereafter he noted that his neck was swollen. He had two more episodes of vomiting before entry. He had never had jaundice, ascites or ankle edema. The appetite had been poor, but there had been no dysphagia. No other contributory information was elicited.

On physical examination the patient was obese, flushed and in respiratory distress. The temperature was 101°F, the pulse 104, and the respirations 32. The blood pressure was 110/66. On palpation there was creptus over the mandible, the entire neck and the anterior chest to the costal margin. The trachea was in the midline. There were prominent superficial veins over the right anterior chest. The anteroposterior diameter of the chest was increased. Tactile fremitus and resonance were decreased over the left lower lobe, and the breath sounds were faint. No rales were heard. The remainder of the chest was hyperresonant. The area of cardiac dullness was obliterated, but this finding was difficult to evaluate because of the emphysematous chest. The heart sounds were faint, and no murmurs were heard. Except for slight upper abdominal tenderness, there were no noteworthy physical findings.

No abnormality of the urine was noted. Examination of the blood revealed a hemoglobin of 80 per cent and a white-cell count of 3450, which rose to 15,200 on the 2nd hospital day. Examination of the sputum revealed no tubercle bacilli. The vomitus and a stool were guaiac negative. The blood Hinton reaction was equivocal. The venous pressure in the antecubital fossa was equivalent to 150 cm. of water, and the arm-to-lung circulation time, which was tested with paraldehyde, was 15 seconds. Roentgenograms of the chest and of the neck were regarded as consistent with mediastinal and subcutaneous emphysema. An abdominal film was within normal limits. An electrocardiogram showed sinus tachycardia, with slightly low origins of the ST segments in Leads 2 and 4.

On bed rest the temperature quickly returned to normal and the dyspnea disappeared. In the hope of hastening resorption of air from the mediastinum, oxygen therapy was instituted.

About 14 hours after entry the patient again became dyspneic and the blood pressure fell to 80/40, where it remained until shortly before death. On the 2nd hospital day crepitant rales were heard at the lung bases. Because of the rales and the elevated white-cell count, although the temperature was normal, sulfapyrazine was given in full doses orally. A roentgenogram of the chest was interpreted as showing atelectasis of the right and left lower lobes. Later in the day the patient became violent, tearing away his oxygen mask repeatedly. The pulse rose to 130 and was of small amplitude. Dyspnea followed by cyanosis ensued, and since the signs of mediastinal emphysema were still marked it was believed that the only therapeutic measure with a reasonable chance of success was mediastinal decompression.

The patient was removed to the operating room where the superior mediastinum was entered digitally after a low collar incision had been made. There was some egress of air, cultures of the mediastinum were made, and the wound was closed about a rubber dam. For about an hour the patient appeared to breathe more easily and to be making slight improvement. Despite supportive measures, however, he slowly weakened and died 9 hours after operation and 48 hours after the onset of symptoms.

Autopsy. At post-mortem examination subcutaneous and mediastinal emphysema was found as clinically described. The essential abnormality was a longitudinal linear rupture of the esophagus, 2 cm long, just above the esophageal hiatus of the diaphragm. It communicated with a cavity containing foul, dark-brown fluid, which bulged against the posterior aspect of the pericardium and was walled off from the left pleural cavity by fibrinous adhesions. Microscopically there was no evidence of peptic ulceration of the esophagus. Gas-forming bacilli were not found in the swabs taken from the chest at operation or at autopsy, although suitable procedures for culture were carried out. Additional findings were bilateral pleuritis due to a Type 5 pneumococcus, congestion and edema of the lungs, with bronchopneumonia, and moderate alcoholic cirrhosis of the liver. Death was attributed to respiratory embarrassment.

The pathogenesis, pathological physiology, clinical manifestations, diagnosis and treatment of mediastinal emphysema have recently been reviewed by Hamman,⁴ who indicates the need for mediastinal decompression when signs of high pressure within the mediastinum manifest themselves, although in the absence of these signs rest and symptomatic measures suffice. Hamman lists four possible routes along which air may reach the mediastinum through the fascial planes of the neck, through a perforation of the trachea, bronchus or esophagus, from the retroperitoneal space, and from the interstitial tissues of the lung. The entrance of air into the mediastinum via the second route rarely occurs, but Hamman further states:

No doubt at times air may enter the mediastinum through a perforation of the esophagus. However, where this accident occurs there is always infection and the serious symptoms of infection obscure the lesser symptoms that may arise from a small amount of air entering the mediastinum.

This statement seems somewhat at variance with the findings in Case 2, indeed, McWeeny² described emphysema as one of the most striking and constant findings in spontaneous rupture of the esophagus. Ridgway and Duncan,³ in a review of the literature, found emphysema present in a half to two thirds of the cases.

Case 1 provides an example of uncomplicated mediastinal emphysema, although it may be questioned whether it should be classified as an example of spontaneous mediastinal emphysema (Hamman's syndrome) or whether it should be excluded from the spontaneous type on the basis that fifteen minutes or more prior to the onset of pain the patient had experienced increased intrathoracic pressure associated with coughing and vomiting. The recurrence was known to have happened without any unusual exertion while the patient was in bed in the hospital. Thus it was clearly spontaneous. Regardless of classification this case illustrates the dramatic improvement that occurs with decompression of the mediastinum when the tension within the mediastinum is so great as to embarrass the circulation.

Case 2, which to those in attendance simulated Case 1, was nonetheless clearly one of spontaneous rupture of the esophagus. The findings were typical of the classic descriptions of the condition,^{2,4} the patient being a man, in middle life and alcoholic. Vomiting and retching immediately preceded the illness, which was characterized by a sudden onset, pain in the lower chest and upper abdomen, and shock, with dyspnea and subcutaneous emphysema. Spontaneous mediastinal emphysema, however, occurs in both sexes, alcoholism is not a factor and the condition arises without apparent precipitating factors. In spontaneous rupture of the esophagus—the term "spontaneous" being used rather loosely, but serving to exclude external trauma—violent retching and vomiting, often following the ingestion of an extraordinarily large meal, usually precede the attack. Both emphysema and esophageal rupture have a sudden onset, pain in the former being restricted to the chest, but in the latter, upper abdominal pain, sometimes with a boardlike abdomen, is found in addition to the chest pain. The pain in both syndromes may be aggravated by breathing, but marked thirst and shock are suggestive of esophageal rupture. The extent of emphysema is not of aid in the differential diagnosis, in fact, after esophageal rupture, it has been observed to involve the whole body. Aspiration of the chest through a needle may clinch the diagnosis by revealing the presence of gastric juice or food particles.

The course of spontaneous mediastinal emphysema is usually benign, but, as Hamman states, prompt decompression of the mediastinum may prove life-saving if the venous return to the heart becomes seriously impeded. In contrast, early intervention in spontaneous rupture of the esophagus seems mandatory, although closed drainage of the pleural cavity,⁴ with chemotherapy, may be the procedure of choice.

A few additional points regarding spontaneous rupture of the esophagus may be of interest. This syndrome appears to bear a considerable relation to that described by Mallory and Weiss,^{5,6} in which

NEW HAMPSHIRE MEDICAL SOCIETY

Proceedings of the One Hundred and Fifty-Fifth Anniversary

THE scientific session of the New Hampshire Medical Society convened at 9 30 o'clock on the morning of May 14, 1946, with President Richard W Robinson, of Laconia, presiding

The first item on the program was a motion-picture film entitled "Angina Pectoris," presented through the courtesy of Brewer and Company, Incorporated. The President introduced Dr Paul C Barton, medical director of Brewer and Company, who before the war was director of the Bureau of Investigation of the American Medical Association and during the war served as executive officer of the Procurement and Assignment Service. Dr Barton presented the motion picture. A paper "Autopsy Service — Mary Hitchcock Hospital" was then presented by Dr Ralph E Miller, of Hanover. This was followed by a paper by Dr Edwin B Astwood, of Boston, Massachusetts, entitled "Present Status of the Medical Treatment of Thyrotoxicosis." Dr Louis H Bauer, a trustee of the American Medical Association, then presented a paper "The Medical-Care Problem in the United States." The morning session was concluded at 1:00 p m.

The afternoon session opened with the awarding of fifty-year certificates to Dr H Sheridan Baketel, of Greenland, and Dr Oscar C Young, of Charlestown. Dr Baketel, on receipt of his certificate, spoke as follows:

The presentation of this certificate, commemorating my continuous membership in the New Hampshire Medical Society for fifty years, is fraught with especial significance.

To some men, it might merely mean that they had been in the Society for half a century, exactly as if they had voted the same national ticket for a similar period or carried the same watch. To me, this occasion reaches deeply into my inner consciousness. When I was a small boy in Greenland, riding with my medical idol and inspiration, the late Dr William Oliver Junkins, of Portsmouth, I learned that in taking on the great responsibilities of medical practice, the physician is duty bound to make himself a living part of his profession. This fact was accentuated in my mind while in Dartmouth. The two men who then had such a major part in shaping the minds and ideals of medical students, Drs Carlton P Frost and William T Smith, impressed us with the necessity of allying ourselves with the Society at the earliest opportunity — advice that I followed.

Next to the award of my medical degree in 1895, my proudest moment was the day I received from the secretary of the New Hampshire Medical Society, and one of my most respected Dartmouth professors, the late Dr Granville P Conn, the certificate of membership, dated June 7, 1896. That parchment is one of my most treasured possessions today.

I belong to fifteen or more medical associations and am proud to be a life fellow of the American College of Physicians, but the pleasure of election to these professional groups was never accompanied by the thrill that coursed through my body on that memorable June 7.

Destiny decreed that the past forty-four years should be spent in New York City or adjoining New Jersey, and although I was active there as a practitioner, medical-school professor, editor and research worker, my spiritual self was ever in the Granite State.

My beloved father, the late Rev Dr Oliver S Baketel, brought his family from our native Ohio to Newfields in 1877, and there at the age of four my interest in the State was aroused. It was enhanced at Portsmouth High School, Phillips Exeter Academy and Dartmouth College, where we were taught to venerate the Granite State.

New Hampshire became almost an obsession. I have always read *The Union*, which has daily followed my peregrinations into exotic climes as well as being delivered at home. To me, except by the accident of birth, I am a New Hampshireite to the very core.

One can easily imagine my delight, when in 1940 it became possible to acquire a venerable house on the Parade in Greenland, nearly opposite the old parsonage in which I had passed such a happy young boyhood, and in being near Portsmouth, where many of my formative years were delightfully passed.

In looking about this group, I miss the faces of some of the medical giants of the days when I joined the Society. Barry and Parsons, of Portsmouth, Sullings and Walker, of Concord, McQuesten and Greeley, of Nashua, Flanders, Boutwell, French, Towne and Robinson, of Manchester, Jarvis, of Claremont, Prouty, of Keene, Staples, of Franklin, Smith, of Hudson, McGregor, of Littleton, Boynton, of Lisbon, Mitchell, of Epping, and Nute, of Exeter, to mention only a few. It is a real satisfaction to have known those men who have now passed away, and many other of the splendid physicians who then upheld the dignity of the New Hampshire profession as true followers of Aesculapius.

For these reasons, I am proud to accept the certificate of fifty-year membership.

As I wrote not long ago in *The Trosbadour*: "It is my hope that from my Greenland home, I can continue to look out over life calmly and steadfastly, until the world for me loses itself in the twilight of time and eternity."

The President then requested the delegates from other New England states to stand up and make themselves known.

The report of the House of Delegates was given by the secretary-treasurer, Dr Carleton R Metcalf.

Dr Robinson then presented the president-elect, Dr Ralph W Tuttle who acknowledged the applause of the audience.

President Robinson spoke as follows:

I wish to emphasize something that Dr Metcalf mentioned in the report of the House of Delegates, because I think it is one of the most important projects that the Society as a whole has to consider at the present time. Since we have a small society that is quite well integrated, we have an unusual opportunity to do exceedingly worthwhile and helpful work for the whole of the medical-care problem in this country, if we can undertake, on a voluntary insurance basis, the care of the indigent. The problem has been given some consideration, and it seems feasible to work out a scheme that will be satisfactory both to the welfare agencies and to the medical profession in the State, with the thought that we shall no longer have to be subject to the fees that we have charged for the rendering of such service, on a basis that belittles, in some ways, the medical profession. Of course, during the depression, it was perfectly proper, but because we established a

precedent, evidence that the present fee is being thought of as a proper fee for minimum medical care has grown up in the minds of the people that administer the program.

I should like to see that situation altered and to have the indigent cared for on the same basis as the minimal service charge that we make in the indemnity policy of the Blue Shield. Unfortunately, whereas the co-operation as a whole throughout New Hampshire has been good, there are certain physicians who have not believed that their own opinions regarding this means to take care of the costs of medical care are justifiable. If we could even get the co-operation of such men to the extent that they would be willing to try this as an experiment, so that we could get co-operation throughout the State, it would be possible for us to go ahead with this program. So long as there is any part of the State that is not co-operating, of course, it is apparent that the welfare agencies cannot take up their end of this particular scheme.

Another point that should be emphasized is that the Blue Shield plan that we are operating in New Hampshire is your plan, it does not belong to one physician but to every physician. The Blue Shield, which is simply the physical agent of the physicians in the State, can be altered as policies can be altered, on the basis of any justifiable and reasonable recommendations. You men should consider yourselves welcome to all the meetings of the professional sessions of that organization, and I believe that the directors of the organization want and hope for all possible criticism, because the only desire they have is to make the thing work, both to the benefit and satisfaction of the profession and to the satisfaction of the people that we try to take care of on that basis.

Dr Lendon Snedeker, of Boston, chairman of the Massachusetts Committee of the American Academy of Pediatrics, then spoke as follows:

I am speaking for Dr Colin Stewart, and I am sorry that he could not be here today. I am the executive secretary for the study of the American Academy of Pediatrics in Massachusetts. The study of child health services that the Academy has started is an attempt to obtain a physician's estimate of child health in the United States—facilities for serving children and their extent and location, such as those found in hospitals and in clinics and other health services outside institutions, including the schools. The study is also attempting to find out the contribution to health service to children made by doctors and dentists in every state, and is looking into the question of pediatric education, a topic that is being handled on a national level.

The completion of a project of this sort will take some time, probably another year and a half. Headquarters have been set up in Washington, and Dr John Hubbard, formerly of Boston, is the director for the study. A national committee, headed by Dr Warren Sisson, of Boston, is responsible for the over-all conduct of the study, for which a budget of nearly half a million dollars has been raised. Already, over thirty states have been organized and have started on the job, successful completion of the project appears possible.

Dentists are being reached through the state dental societies in general. Hospitals are being reached by the pediatricians and physicians around the country and the district health officers. The nurses and the doctors responsible for local health services are looking into clinics and extramural facilities.

The Academy has gone on record as being against the present health legislation before Congress, on which it believes this study, and the knowledge that it is being carried out, will have some deterrent effect. It also expects that the information disclosed by this study will be used on both national and state levels for laying a sound basis for any future health legislation that may come about. Much of the planning is up to physicians, and the way to achieve sound planning is for the doctors to get the facts. We are therefore asking you, when the questionnaire comes around, to give us facts on which we can say that this is what the doctors of the country are doing all the time for the children and the children's health services.

Dr Forrest J. Drury, director of the New Hampshire Veterans Service, spoke as follows:

I was glad this morning to hear Dr Bauer state that it was the policy of the present medical officials of the Department of Medicine and Surgery of the Veterans' Administration to keep the physician-patient relation and to provide care for veterans for their service-incurred disabilities, in their own communities and by their own physicians. That is exactly what we wish to do.

We shall authorize any physician registered in New Hampshire to care for any veteran in his community if that physician will co-operate with us in the very necessary paper work. I know that they will immediately say, "red tape," when they see a government form, but we have reduced that, we believe, to the irreducible minimum of forms, and I doubt that we will have any more forms to fill out than the Blue Shield has. We believe that our fee table is comparable to that of the Blue Shield.

If any veteran reports to any physician in the state with a letter that is sent to every veteran when his case has been adjudicated and grants service treatment for a service-connected disability, you are perfectly safe in going ahead and rendering the treatment, if you will report that fact to my office within five days after treatment is rendered. I must have that information. We work on a budget, and I must record the case on the budget within five days.

Veterans are entitled to hospital treatment in civilian hospitals in emergencies, but only for service-connected disabilities, the time consumed in getting the patient to a veterans' hospital and the distance must be considered to be dangerous. Such facts must be reported to my office within twenty-four hours. With outpatient reporting, five days are allowed. But when veterans are placed in hospitals without prior authority first, the case must be reported to my office within twenty-four hours. It is always best to get the authority beforehand.

We have sent letters to every physician on our list, with the probable exception of some men returning from the service, regarding payment of fees for examinations to determine the need for hospitalization. Until last October, examinations for non-service-connected disability could not be paid for. That meant that the doctors throughout the State were doing a great deal of work, and either the veteran paid for the examination or the doctor did not get paid for it. Under the new setup, however, and under a ruling last October, if a doctor is making an examination to determine the need for hospitalization, we can pay a fee of \$3.00, and if the call is made between 7:00 p.m. and 7:00 a.m. the fee can be \$5.00.

We recently sent letters to all physicians, telling them of our twenty-four-hour service. There is a memo on call of all night in the office and on Sundays and holidays. Therefore, the number of the Veterans' Administration can be called any time of the day or night, seven days in the week.

Another point Dr Bauer mentioned was the fact that these services exist in some states. There are two different setups. One is known as the New Jersey and the other as the Michigan setup. I hope that this society, some time in the near future, may see fit to set up a similar service. I prefer the Michigan to the New Jersey plan. The latter is not greatly different from the plan in New Hampshire, except that the society furnishes the names of physicians who have agreed to work on this plan. The Veterans' Administration sends out the forms. Under the Michigan plan, a contract with the Veterans' Administration takes care of everything. A physician in the veteran's community is designated to take care of the particular condition, the society then bills the Veterans' Administration. That, to my way of thinking, is the ideal setup. Under the Michigan plan, we get the names from the state society, instead of individually or from hospital staffs.

I should like to say that if there is any group of physicians, hospital staff, city or county society that would care to have me come at any time to any meeting, to tell them the whole story, I shall be very glad to do so.

Dr John C Leonard, a director of the Joseph Pratt Diagnostic Clinic in Boston, Massachusetts, then presented a paper entitled "Hypertension"

This was followed by a paper by Dr Clay R Murray, of New York, the subject being "Handling of Common Injuries to the Knee Joint"

Dr John T King, of Baltimore, professor of Medicine at Johns Hopkins University School of Medicine then presented a paper entitled "Acute Chest Episodes Caused by Pulmonary Embolism Differential diagnosis and treatment"

A financial report from the Trustees for the period beginning January 1, 1945, and ending December 31, 1945, was then presented, as follows

GENERAL FUND

Receipts

Balance on hand January 1, 1945	\$4,775 11
Nashua Trust Company interest	6 70
Portsmouth Trust and Guarantee Company interest	24 56
New Hampshire Savings Bank interest	26 37
U S Series G bonds interest	125 00
Total	\$4,957 74

Expenditures

U S Series G Bonds	\$2,000 00
Cash balance December 31, 1945	\$2,957 74
U S Series G bonds	5,000 00
Total Fund	\$7,957 74

BARTLETT FUND

Receipts

Balance on hand January 1, 1945	\$2,998 92
Portsmouth Savings Bank interest	71 04
U S Series G bonds interest	50 00
Total	\$3,119 96

Expenditures

Trustees of Dartmouth College	
Repairs on animal pen at Medical School	\$1,000 00
Cash Balance December 31, 1945	\$2,119 96
U S Series G bonds	2,000 00
Total fund	\$4,119 96

PRAY FUND

Receipts

Balance on hand January 1, 1945	\$291 08
Strafford Savings Bank interest	4 37
U S Series G bonds interest	25 00
Total receipts and cash balance December 31, 1945	320 45
U S Series G bonds	1,000 00
Total fund	\$1,320 45

BURNHAM FUND

Receipts

Balance on hand January 1, 1945	\$1,064 01
N H Savings Bank interest	21 28
U S Series G bonds interest	25 00
Total receipts and cash balance December 31, 1945	\$1,110 29
U S Series G bonds	1,000 00
Total fund	\$2,110 29

BENEVOLENCE FUND

Receipts

Balance on hand January 1, 1945	\$3,239 81
Dr Metcalf	100 00
N H Savings Bank interest	65 51
U S Series G bonds interest	75 00
Total receipts and cash balance December 31, 1945	\$3,480 32
U S Series G bonds	\$3,000 00
Total fund	\$6,480 32

HOWARD N KINGSFORD, M D
GEORGE C WILKINS, M D
SAMUEL T LADD, M D

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

CASE 32431

PRESENTATION OF CASE

A fifty-four-year-old woman entered the hospital because of fecal vomiting

Five days before admission the patient had a sudden onset of severe, steady upper abdominal pain. She was seen by a physician about an hour later, when she was lying across a bed on a hot pad sweating and in such pain that she could not talk clearly but moaned and changed position frequently, attempting to void, urinate or vomit for relief.

The temperature was 96.4°F, the pulse 64 and the blood pressure 160 systolic, 90 diastolic. The patient had previously been known to have moderate hypertension. The abdomen was soft and nontender, and no scar was present. Peristalsis was minimal. Some time later she gagged in the hope of relief. Despite the administration of morphine, the steady pain continued through the night. On the following day the abdomen was still relaxed and nontender and almost silent. The patient was given 3 mg of Dilaudid and 0.1 gm of phenobarbital, and she slept. She was free of pain that evening and on the next day managed to retain a little food. Two days later she felt better and sat up, but vomited that evening. On the day before and on the day of admission she felt weak and vomited. The vomitus became fecal. Since the third day before admission there had been no pain or fever and the pulse had been slow.

On entry the patient had no pain. She was alert and talkative. The tongue was dry. The heart beat was regular at 80 per minute. The abdomen was slightly distended and tense, without spasms or tenderness. No masses were felt. Peristalsis was active and slightly high pitched, but was thought to be within normal limits. The uterus felt slightly enlarged on vaginal examination.

The temperature was 98.6°F, the pulse 72, and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,500,000, with 11.4 gm of hemoglobin per 100 cc, and a white-cell count of 10,350, with 82 per cent

neutrophils many of which were band forms. The urine gave a ++ test for albumin, and there were 20 white cells and 10 red cells per high-power field. An abdominal film showed gas-filled loops of large and small bowel, one of which appeared distended.

A Miller-Abbott tube was inserted, and the patient passed a comfortable night. On the second hospital day there was slightly less distention, but peristalsis was definitely high pitched. She passed gas and a single, large stool containing old blood. The nonprotein nitrogen was 41 mg per 100 cc, the chloride 89 milliequiv per liter, the protein 6.3 gm per 100 cc, and the amylase 23 units per 100 cc. The white-cell count was 8100. On the third day she felt improved, the heart sounds were regular. The blood pressure was 110 systolic, 60 diastolic. The abdomen was distended, but softer. A soft nontender mass, 6 by 6 cm, was felt above the pubis. Peristalsis was normal. Another plain film of the abdomen showed dilated loops of small bowel in the central portion of the abdomen.

An operation was performed on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR MARSHALL K BARTLETT May we see the x-ray films?

DR MILFORD D SCHULZ The film made at the time of entry shows a gas-filled, dilated stomach and several loops of small bowel below it that are also distended with gas. Apparently some opaque medication was given by mouth some time before entry. The film made two days later, apparently when a barium enema had been given, shows no real obstruction in the colon. I think that there are still a few remaining loops of small bowel that are distended with gas. It looks as if there is some extrinsic pressure on the sigmoid, but there is no evidence of intrinsic disease.

DR BARTLETT Does the colon look normal?

DR SCHULZ Yes, except for the pressure on the sigmoid, which may be just an adjacent viscus.

DR BARTLETT To explain this picture we must find a condition that will account for the onset of extremely severe pain in the upper abdomen, without abdominal findings and without physical findings either at the time of onset or subsequently. The pain disappeared at the end of two days, and the patient had no further pain at any time. She subsequently developed symptoms that seem to point to a mild, incomplete intestinal obstruction. The symptoms did not include pain but she had vomiting that persisted and became fecal. She had peristaltic sounds that became high pitched and suggested a dilated bowel, and she had x-ray findings that are consistent with some type of obstruction. I am sure that if I had seen this patient at the onset of the original pain I should have considered stone in the biliary system, acute pancreatitis, perforation of a hollow viscus and possibly a dissecting aneurysm.

mesenteric thrombosis. It seems to me that we rule out a number of those conditions by the subsequent course of events. I do not see how a lesion of the biliary system or acute pancreatitis could have in this way. I do not believe that the subsequent intestinal symptoms would have developed on that basis.

How about a dissecting aneurysm? Again, I do not believe that the gastrointestinal symptoms could be accounted for in that way. At the end of seven days a large stool containing old blood was passed. Also, later on, a mass appeared that was not felt on admission — pelvic examination was done at that time and did not show it, it developed later. Could this have been something in the lower abdomen such as a twisted ovarian cyst or a volvulus of the sigmoid? I do not believe that either could account for the onset of such severe upper abdominal pain that disappeared completely in two days. It seems to me that we must find some lesion that will cause pain referable to the upper abdomen impairing the blood supply to the bowel in a manner that will allow some bleeding into the intestinal tract, so that that blood will later be passed as old blood, and a lesion that at the same time will give a picture of partial intestinal obstruction. I think that we can exclude the colon on the basis of the symptomatology, and I believe that we must place this lesion fairly low down in the small bowel. I believe that the likeliest thing that occurred in this woman was a mesenteric thrombosis. There are obviously a number of things that do not fit that picture, such as the lack of abdominal signs and the fact that the white-cell count was only 10,000. In spite of that, however, it seems to me that mesenteric thrombosis fits the picture better than anything else I know of, and I shall make that diagnosis.

DR. TRACY B. MALLORY: Is there anyone who would like to make a suggestion?

DR. MAURICE FREMONT-SMITH: Could the patient have had an intussusception that cleared up?

DR. BARTLETT: I think that she could have — one that was spontaneously relieved?

DR. FREMONT-SMITH: Yes, but in adults intussusception is usually associated with polyps or carcinoma.

DR. BARTLETT: It is usually associated with some tumor.

DR. MALLORY: One would probably expect previous attacks of incomplete obstruction in such a case.

A PHYSICIAN: How about internal hernia?

DR. BARTLETT: Do you mean by that a loop caught under a band?

A PHYSICIAN: Yes.

DR. BARTLETT: I think that she could have had that, but the symptoms were mild and the obstruction was incomplete. I also think that that would be less likely to give bleeding in the bowel.

DR. MALLORY: Dr. Welch, will you tell us your opinion before operation?

DR. CLAUDE E. WELCH: Perhaps I should first apologize for the surgical treatment. One might wonder why operation was delayed for four days after the patient came to the hospital. When she came in I could not even be sure that she had intestinal obstruction. She had a history of severe pain occurring three hours after drinking some cocktails, described by the physician, who had sampled them himself, as "sulfuric acid." She was so well at the end of almost a week's sickness that when she came to the hospital I thought that perhaps she had gastritis. We elected to treat her conservatively. At the end of twenty-four hours, it was obvious that there was obstruction. There really was fecal material coming out of the Miller-Abbott tube. We decided to give a barium enema and to study the situation further before exploration. As time went along the preoperative diagnosis favored by Dr. Arthur W. Allen was an intussusception because of the presence of the abdominal mass and the bleeding by rectum, together with intestinal obstruction. There were several votes in favor of the diagnosis of Meckel's diverticulum. In other words we all thought of the rare lesions and we also thought that, whatever the cause of the obstruction, it was a nonstrangulating type.

DR. MALLORY: Will you describe the operative findings?

DR. WELCH: When the abdomen was opened bloody fluid was immediately apparent. This mass that had been variously interpreted as fibroid uterus or some lesion associated with the bowel was a mass of gangrenous bowel that had been caught behind a simple band. As soon as the band was cut, the whole intestinal tract righted itself, but it was necessary to resect this entire loop of bowel. The patient had had no previous abdominal operation and no previous infections anywhere in the pelvis. We could not make out the cause of the bands but there were two present, one of which had caused the trouble.

CLINICAL DIAGNOSIS

Small-bowel obstruction

DR. BARTLETT'S DIAGNOSIS

Mesenteric thrombosis

ANATOMICAL DIAGNOSIS

Strangulation of bowel by adhesive band.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The operative specimen we received showed nothing but gangrenous bowel. No cause was ever determined for the adhesive band.

DR. ALFRED KRAVES: What was the primary lesion?

DR MALLORY An adhesive band in a woman with no previous operation and no infection. There was secondary thrombosis of the mesenteric vessels.

DR FREMONT-SMITH If we knew that she had a band, should she not have been operated on at the beginning?

DR WELCH The point is that when she was first seen outside she should have been operated on at once. Then she would have been well and been home three weeks earlier. As time went on her condition became worse, and operation without preparation might have been fatal.

DR EARLE M. CHAPMAN I am sorry to have arrived late for this discussion, but perhaps I can clarify things a bit. This woman was quite well until a Sunday night when she drank the sour cock-tails at 6:00 and then had the agonizing abdominal pain that started about 10:00. I was awakened to see her at midnight, and the first thing I considered was gastritis severe enough to cause erosion or even perforation, but she had had such a normal abdomen without any scar on it that even a surgeon would have hesitated to operate at that time. I returned to Boston and she, being a Christian Scientist, was attended by the healer several times, but when fecal vomiting appeared the family overruled faith treatment and called in a neighborhood surgeon, who advised immediate operation. The family telephoned me — hospitalization here was advised, and I still think that the four-day delay in operation was wise treatment. At entry she was sick and vomiting and had an elevated nonprotein nitrogen and a low blood chloride, with supportive treatment she was in much better condition and made an amazing postoperative recovery.

CASE 32432

PRESENTATION OF CASE

A twenty-year-old girl entered the hospital complaining of a tumor on the collar bone of one month's duration.

The patient stated that she had always been in excellent health until about a month before entry, when she noted a small swelling located at the right sternoclavicular junction that was not tender or red and had not bothered her. It had increased rather rapidly in size, until it reached the size of a golf ball. There had been no weight loss.

Physical examination revealed a well developed and well nourished obese girl who did not appear ill. Positive physical findings were limited to the skin and the right clavicle, where there was a hard tumor, about the size of a golf ball, located on the superior portion just lateral to the sternoclavicular joint. It was slightly movable and was less hard on top than at the base, seeming to be attached to the clavicle.

The temperature was normal, and the blood pressure was 90 systolic, 60 diastolic.

Examination of the blood showed a red-cell count of 5,020,000, with 97 per cent hemoglobin and a white-cell count of 7500, with 52 per cent neutrophils, 38 per cent lymphocytes, 7 per cent monocytes and 3 per cent eosinophils. The red cells and platelets were normal. The blood Hinton test was negative.

X-ray films of the right clavicle revealed a destructive lesion, involving the proximal 5 cm of the clavicle with destruction of the cortex in the involved area, which extended up to the sternoclavicular junction. A film of the chest showed the lungs to be clear.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR ERNEST M. DALAND The physical examination was essentially negative, with the exception of the lesion over the clavicle, which was revealed, on x-ray examination, to involve the clavicle. I believe that it comes down to a differential diagnosis of conditions arising in the clavicle.

May we see the x-ray films?

DR JAMES R. LINGLEY This is the lesion involving the medial end of the clavicle. I cannot add anything to the description given in the record. It appears to be destructive and has broken through the cortex.

DR DALAND Is there destruction of the upper cortex?

DR LINGLEY I think that there is probably destruction all the way through.

DR DALAND Has the lesion broken through the end of the bone?

DR LINGLEY The articular cortex looks intact. It has broken through anteriorly.

DR DALAND We must consider inflammatory lesions and tumor. The inflammatory lesions that could be involved include osteomyelitis, which I think we can rule out, since the white-cell count was normal and the patient was in fairly good general physical condition. Tertiary syphilis must be thought of immediately, because this is a frequent position for a gumma. The blood Hinton test was negative, and that fairly well rules out that diagnosis. Tuberculosis should also be considered, but it seems to me that one would expect to find complete destruction of the clavicle, including penetration through the articular surface. I think that a tuberculous process would have worked in around the sternoclavicular joint rather than have projected out as an external tumor. I believe that we can rule out any inflammatory condition.

The tumors most frequently encountered in the clavicle are probably the giant-cell tumors. In a giant-cell tumor one expects to find an expansile tumor with nearly equal vertical and horizontal diameters. Signs of expansion of the bone would have been observed before any break in the cortex, and the history would probably have been longer.

in one month with symptoms I think that we can rule out giant-cell tumor. An enchondroma could have occurred but again I think that there could have been evidence of bone expansion before rupture of the cortex, as well as a more distinct outline of the tumor. Osteogenic sarcoma is always a possibility in any bone, there is no bone where it cannot occur. The appearance of this lesion is suggestive of it, in that there was a break in the cortex on both sides, with an external tumor mass. There was no ray formation that I can make out and that is one of the characteristic signs of osteogenic sarcoma. There are no typical signs in an early case, however, and osteogenic sarcoma is a distinct possibility. I doubt that an eosinophilic granuloma could have produced an external tumor mass of this size with a bone lesion no larger than this. There is no note that there was any expansile pulsation, such as one expects in hemangioma destroying bone, and the external surface did not suggest hemangioma. We must consider metastatic cancer. Carcinoma of the breast can metastasize to the clavicle, as can many other types of carcinoma. This girl was only twenty, however, and the chances are against it. Physical examination apparently did not reveal any other disease suggesting a primary focus, and I think that metastatic carcinoma can be ruled out.

The probability is that this was a lymphoma. Lymphoma does occur in the clavicle as a solitary lesion. I recall a solitary lymphoma of the mid-portion of the clavicle that I resected about twelve years ago. I inserted a bone graft, and the patient remained well with no secondary lymphoma. The physical examination in the case under discussion also did not show any other sign of lymphoma. My belief is that this will turn out to be a lymphoma.

DR. LINGLEY: I should like to ask Dr. Daland if he would consider a Ewing tumor?

DR. DALAND: Yes, Ewing tumor should certainly be considered, and I cannot rule it out.

DR. TRACY B. MALLORY: What was your diagnosis, Dr. Lingley?

DR. LINGLEY: I thought that it was either Ewing tumor or lymphoma, and I put the former first.

DR. MALLORY: Dr. Hare, you originally read these films. What did you think about them?

DR. HUGH F. HARE: I thought that it was a lymphoma and put Ewing tumor second.

CLINICAL DIAGNOSIS

Lymphoma of clavicle

DR. DALAND'S DIAGNOSIS

Lymphoma of clavicle

ANATOMICAL DIAGNOSIS

Ewing tumor of clavicle.

PATHOLOGICAL DISCUSSION

DR. MALLORY: The operation mentioned in the record, at the point where the abstract terminates, was a biopsy, which showed a characteristic picture of a Ewing tumor. The patient was then given x-ray treatment by Dr. Hare. Perhaps he will tell us about that stage of the progress.

DR. HARE: When I first saw the patient following the biopsy, the swelling was considerably larger than a golf ball, being about the size of a lemon. We started treatment with large daily doses of 350 r, a total of 2800 r being given to the skin. It caused a skin reaction, and at that time we discontinued treatment. I saw the girl six weeks later, when the tumor had decreased somewhat in size.

DR. MALLORY: About two months following the x-ray treatment the patient again entered this hospital, and it was decided to resect the clavicle. That was done, and I have a photograph (Fig. 1) that I shall show you. The proximal end of the clavicle lies



FIGURE 1

to the right. A large cystic cavity filled with blood and necrotic tissue can be seen. We made many sections throughout that area. We were unable to find any remaining trace of tumor. So far as the morphologic evidence is concerned, the x-rays had apparently completely destroyed the neoplasm.

One always has the alternative of x-ray treatment or surgery in these cases. Does anyone wish to express an opinion in this case? This patient was given a double chance, since she received both forms of treatment in succession.

DR. GRANTLEY W. TAYLOR: This patient's family was anxious that something further be done if possible to improve her chance of cure, because the prognosis given to them following biopsy and x-ray treatment had been pessimistic. Since the tumor was still present and the x-ray evidence of destruction showed a continuing process in the clavicle, it seemed worth while to consider excision of the clavicle. The skin had recovered from the initial radiation reaction and had not yet undergone the late changes that jeopardize healing following surgery through a radiated area. With these facts in mind, the entire clavicle was removed, including the periosteum and the muscular attachments. The pa-

tient made an excellent recovery from operation, and the wound healed primarily. She has returned to work and has excellent function of the arm. There is no evidence of metastasis or recurrence at the present time.

DR. RICHARD H. WALLACE: I should like to ask about the possibility of recurrence with this sequence if the clavicle had not been removed. What assurance is there that there might not have been a few viable cells?

DR. MALLORY: Frankly speaking, none. It would be impossible to rule that out with certainty.

That there had been massive and apparently complete destruction of tumor is all that I can say.

DR. WALLACE: Would there be reasonable assurance that it might not recur, since there was no microscopic evidence of tumor?

DR. MALLORY: I should prefer to have a radiologist's opinion. It is my impression that, in a fair number of these cases treated by x-ray, there has been no recurrence even in the face of metastases. Is that correct?

DR. LINGLEY: Yes, we have had several such cases.

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"A HUNDRED YEARS AGO"

IT HAS long been a custom of certain of our esteemed, if more youthful, contemporaries, particularly those addicted to the daily dissemination of current events, to publish a department that comments briefly on the happenings of an otherwise forgotten era. Thus each day there appears in subdued tones, betokening the softening influence of time, the abbreviated news stories of a quarter century ago, reminding the reader that there has been a past, however colorless, in addition to a troublesome present and a hypothetical future. In view of these attempts to link the present with the past, the *Journal*, sturdy survivor of a hoarier

age,—for even the *Boston Herald* came in only with ether,—has decided to make its own contribution to this factual anthology with its scarcely rivaled opportunities for chronological research, it has determined to dig more deeply into the archives of antiquity and bring forth from time to time, or at approximately lunar intervals, brief excerpts from its own files of a century ago.

The first article of the series appears elsewhere in this issue of the *Journal*, and it should be noted that the leading item in these abstracts of October, 1846, comments on that anesthetizing preparation with the aid of which, no doubt, our previously mentioned young journalistic contemporary was eaned. Even then, the *Journal* was in the fore with the publication of medical discoveries of importance. Some of these excerpts deal with truths that seem to be permanent, which is less often the case with scientific advances than it is with some of the basic principles of our art. Thus, with the reference to the poor chirography among medical men, this is as true today as it was a century ago, and is due, obviously, to the policy of putting it up to the apothecary to compound the prescription the way it ought to be.

These miscellaneous abstracts will serve other purposes than to entertain and to amuse. They will remind us that former days have had their pioneers, their heroes, their men of stature, that the achievements of today are built on the foundations that untold centuries of achievement laid down. While we are entertained, let us also be chastened, for one day we, too, will be of a century that has passed.

The *Journal* is fortunate in that Dr. Reginald Fitz has consented to compile this column. A student of medical history, Dr. Fitz brought to his term of office as president an unusual devotion to the interests of the Massachusetts Medical Society, as well as a knowledge of its traditions.

THE PATIENT AND THE TRUTH

THE question whether a patient with malignant disease should be told the truth, the whole truth and nothing but the truth is not easy to answer. The

subject is thoroughly discussed in two papers in the June issue of the *Annals of Internal Medicine*.^{1,2}

The chief difficulties in answering this question arise from the facts that the psychologic make-up of one patient differs from that of another, that legal responsibility is involved and, finally, that the physician himself does not always know what is the truth — the best may be mistaken. A family will forgive him if he says that the patient is going to live and the patient subsequently dies — for all men die, but the physician will never be forgiven if he predicts without qualification a fatal outcome and the patient then proceeds to get well. Furthermore the intricacies of medical terminology are such that the doctor is often forced — in telling the truth — to use lay terms that are, in themselves, scientifically inaccurate to convey to the patient his idea of the truth, and thereby he may defeat his own purpose and end merely by confusing or, from a legal point of view, by misleading the patient.

Certain principles seem reasonably well established. Some responsible friend or relative of the patient must be apprised of the facts in so far as they are known. No operation, unless it be an emergency life-saving measure, may be done without the patient's consent. No misstatement of facts or evasive answers may be given if the purpose is to serve the physician's personal interests or financial gain, nor may an operation be performed for like reasons. A physician may be liable if he makes a positive but erroneous diagnosis. It is rather generally agreed that a doctor suffering from one or another form of malignant tumor should be so told, but from this point on there is no unanimity of either legal or non-legal opinion regarding how much or how little should be said.

It may seriously be questioned whether it "usually does good to patients to tell them that the outlook is hopeless."¹ It seems truer that "an insight gained gradually is less likely to cause intense mental anguish than knowledge gained abruptly of one's imminent demise."² A few there are who can face the truth with equanimity. There are some, of course, who must be told the truth because their personal or professional responsibilities are such that their affairs must be put in order. But even here,

if some responsible member of the family or some close friend has been informed about the facts, it is not often that the patient need be directly told by the physician.

It may be necessary or advisable to tell a given patient that he has cancer in order to persuade him to undergo what is believed to be the necessary therapeutic measures, but at the same time the word "cancer" may so frighten a patient that he refuses treatment, — so imbued is the lay mind with the idea that cancer is incurable, — and the use of such a word as "tumor" or "mass" often serves better to adjust the patient's therapeutic future.

The question whether a physician if asked by a patient with cancer "Have I cancer?" must necessarily answer "Yes" is a moot one. It is doubtful whether a suit would lie were the physician to skillfully by-pass the question, provided, of course, that some responsible member of the family knew the facts.

The question of prognosis is also a difficult problem. At best one can deal in broad generalities. Neither the average nor the mean necessarily applies to the individual case unless the extremes are so close to each other that the difference is negligible. A patient with malignant or pseudomalignant disease is usually satisfied with the statement that the condition is a serious one, that certain therapeutic measures are advisable and that benefit will accrue. As time passes the patient either fails progressively without fully realizing it or, by himself, comes to recognize that he will have the disease all his life. From that point the transition to a realization that he will die of the selfsame disease is an easy one, and the experienced physician is able to tell when such knowledge has been gained. When it has, the patient seldom speaks of it, the doctor need not.

If a physician has followed a course sincerely designed for the patient's best interests, if he has told some responsible person the facts and if he has informed the patient that the condition is a serious one, no court would judge him derelict in his duty.

REFERENCES

1. Lund C C. Doctor, patient, and truth. *Ann Int Med* 24 955-959, 1946
2. Smith, W S. Legal privilege on therapeutic grounds to withhold specific diagnosis from patient sick with serious or fatal illness. *Ann Int Med* 24 960-967, 1946

HUNDRED YEARS AGO

Strange stories are related in the papers of a wonderful preparation in this city, by administering such a patient is affected just long enough and just powerfully enough to undergo a surgical operation without pain — Benjamin Waterhouse, M D, died recently at the patriarchal age of ninety-two at his residence in Cambridge. During the active part of his life very few physicians have held a more conspicuous place in the public observation. A lecture which he delivered about 1805 to the Harvard undergraduates on the custom of smoking cigars is supposed to have had great influence in whatever diminution of that practice was consequent on its publication. He was an early and decided advocate for the introduction of the practice of vaccination into this country and always esteemed it one of his proudest laurels that he was designated the American Jenner — Cholera morbus is spoken of as being quite fatal in the eastern part of New Hampshire. — As a fraternity medical men are proverbial for their bad writing. Some of the manuscripts sent to us would puzzle the chirographical professor to determine whether they were written in English, Chinese or Cherokee. A physician who cannot write should not be allowed to practise, and a man who can write and only scrawls should be regarded as committing a criminal offence — Dr Daniel Drake, of Cincinnati, reports "I have lately assisted in the *post mortem* examination of two patients who died after several weeks of illness with symptoms answering well to Louis' description of Typhoid Fever. This fever may be among our increasing diseases. If so, it is entitled to great attention, just as an invading army should be more vigilantly watched than one which is retreating. Can anyone tell whether those cases of remittent bilious fever which in their latter stages exhibit typhoid symptoms are accompanied by lesions of the ileum?" — A boy seven years old swallowed an open penknife three inches long. The symptoms afterwards were slight. The treatment enjoined was perfect quietude, fomentations, saline febrifuges, sedatives, the occasional exhibition of slight aperients, castor oil etc. On the morning of the sixth day the knife appeared with an evacuation, blade downward, somewhat corroded and not at all improved in appearance by its change of residence. — The increasing population of Boston demands corresponding charities to meet the necessities of the sick and infirm poor. A conviction that another infirmary was required led to the

recent opening of one at 425 Washington Street. This is to be open at all hours so that those who are least able to walk from a remote section of the town will be certain of finding someone to give them desired advice. John B Walker, M D, takes charge of the department of surgery, C E Buckingham, M D, E H Clarke, M D, S Kneeland, M D, and W Henry Thayer, M D, will in turn be in attendance in the management of the medical labors. All operations will be performed gratuitously when necessary and bandages, apparatus etc freely given — A lady ninety years of age residing at Cold Spring has recently cut four front teeth, being the third set, and her eye-sight has so far returned that she can see without glasses. — Some villain has discovered a new agent of iniquity in the way of drugging cigars with narcotics. A boy of five picked up a cigar partly smoked and gave it to a journeyman tailor. He lighted it but after a few puffs, experiencing some uneasy sensations in his head, threw it down. The little boy then tried it, exhibited all the symptoms of violent poisoning and died eighteen hours later. Three professional gentlemen who saw him opined that the cigar had been drugged with some virulent narcotic — A new remedy for strangury is announced. Take 40-60 bees in a tea-cup, pour one gill of boiling water on them and cover the cup securely. When it has stood for about twenty minutes, pour off the infusion and let the patient take the whole as a draught. It is supposed that the material which gives efficacy to the bee tea is the virus ejected by its sting. It remains to be seen whether this virus may not be collected and preserved so as to be employed when the bee itself is not to be obtained — A barrel containing several parts of a human skeleton was found floating in the upper basin of the Mill Dam, Boston, by some boys last week — A Swiss journal states that the bulb of the dahlia when dressed like the potato affords an excellent article of food — We perceive that Medical Societies in several States have already elected delegates to the great convention to be holden in Philadelphia in May next. If we may judge from the spirit manifested at the last convention, we presume that medical men of respectability who may be present will not only have seats accorded to them but the liberty of discussion if they desire it — Extracted from the *Boston Medical and Surgical Journal*, October, 1846

R F

NEW HAMPSHIRE MEDICAL SOCIETY

DEATH

WIGGIN — Henry M Wiggin, M D, of Whitefield, died June 29. He was in his seventy-eighth year.

Dr Wiggin received his degree from Boston University School of Medicine in 1895.

His widow and two sons survive.

MISCELLANY

DR BARTON AWARDED LEGION OF MERIT

Dr Walter E Barton, superintendent of the Boston State Hospital, was recently awarded the Legion of Merit Medal for his work with the Office of the Surgeon General in the rehabilitation of Army patients. Active for fifteen years in the Massachusetts State Medical Service as a psychiatrist, Dr Barton received the award for his work in organizing and developing the reconditioning program for convalescing patients. As a lieutenant colonel in the Army Medical Corps, his specific services in shaping the doctrine and policy of the four interrelated services of occupational therapy were instrumental in furthering Army medical care.

NOTE

Dr Lloyd C Fogg, formerly associate professor of microscopic anatomy, Boston University School of Medicine, has been appointed registrar of the School. Dr Fogg assumed his new duties at the beginning of the current academic year.

CORRESPONDENCE

ERRATUM

To the Editor I wish to call attention to an error that crept into my manuscript "Surgery of the Innominate Artery," which was published in the July 18 issue of the *Journal*.

On page 74, near the bottom of the first column, I referred to "Burrell, of Philadelphia." Actually, Dr Burrell was a clinical professor of surgery at Harvard and a resident of Boston. The error came about because the transcription in which his case was published was for the meeting of the American Surgical Association held in Philadelphia in 1895. Dr David Cheever pointed out this error to me.

789 Howard Avenue
New Haven, Connecticut

GUSTAF E. LINDSKOG, M D

NOTICES

ANNOUNCEMENTS

Dr Edward A Adams announces that Dr Robert S Thomson is associated with him for the practice of general surgery at 44 Oliver Street, Fitchburg.

Dr Norman H Boyer, having returned from military service, announces the reopening of his office at 29 Bay State Road, Boston.

Dr Thomas E Chretien has returned from naval service and announces the opening of an office for the practice of general medicine at 435 Wolcott Street, Auburndale.

Dr Clito R Damiani announces the opening of an office at 16 Norwich Street, Worcester, for the practice of dermatology.

Dr William H Holtham, having returned from military service, announces the reopening of his office for the practice of urology at 270 Commonwealth Avenue, Boston.

Dr Philip A Isaacson, having returned from military service, announces the opening of his office for the general practice of medicine at 717 Main Street, Fitchburg, Massachusetts.

Dr G S Nossaff, having returned from military service, announces the opening of an office at 38 Congress Street, Milford, succeeding Dr Perry E Joslin.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday November 5, at 8 15 p m. Dr Reginald H Smithwick will speak on the subject "Operative Measures for the Relief of Hypertension."

CUTTER LECTURE

The Cutter Lecture on Preventive Medicine will be given by Sir Lionel Whitby, Regius Professor of Physics, University of Cambridge, England, at 5 p m on Wednesday, November 6, in the Amphitheater of Building D of the Harvard Medical School. His subject will be "The Hematological Effects of Irradiation."

The medical profession, medical and public-health students and others interested are cordially invited to attend.

SUFFOLK DISTRICT MEDICAL SOCIETY

The fall dinner meeting of the Suffolk District Medical Society will be held at the Harvard Club of Boston on Saturday, November 9, at 7 00 p m. Dr Shields Warren will speak on "The Physiological and the Pathological Effects of the Atomic Bombs," and Dr Joseph C Aub will speak on "Isotopes in Clinical Research."

Members of the district society and their wives, as well as young people of high-school and college age whose parents are members, are cordially invited to attend. Tickets for the dinner and cocktails (\$3 00 per person) must be purchased in advance by sending cash or a check to Dr Richard S. Eustis, 319 Longwood Avenue, Boston 15, before November 7. After this date other members of the Massachusetts Medical Society, their wives and young adult members of their families, may apply. Cocktails will be served at 6 30 p m.

AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

The third American Congress on Obstetrics and Gynecology will be held September 8 to 12, 1947, in St. Louis, Missouri. All the meetings and the scientific and technical exhibits will be held in the Municipal Auditorium.

Although the third congress is similar in scope and program to the two previous meetings, it will be larger in every way. The program is being made up to appeal to specialists in obstetrics and gynecology, to general practitioners interested in those fields, to hospital administrators and to nurses, as well as to public-health physicians and nurses.

The morning sessions of the congress on September 12 will be given over entirely to the National Federation of Obstetric and Gynecologic Societies. An evening speaker of national prominence will present his viewpoints to a joint meeting of the congress, the federation and the general public.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, OCTOBER 31

FRIDAY, NOVEMBER 1			
*10 00 a m - 12 00 m	Medical Staff Rounds	Peter Best	Brigham Hospital
MONDAY, NOVEMBER 4			
*12 15 - 1 15 p m	Clinicopathological Conference	Peter Best	Brigham Hospital
TUESDAY, NOVEMBER 5			
*12 15 - 1 15 p m	Clinicorontgenological Conference	Peter Best	Brigham Hospital
8 15 p m	Greater Boston Medical Society	Auditorium	Beth Israel Hospital

(Notices continued on page xx)

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ISLET-CELL TUMOR OF THE PANCREAS WITH HYPERINSULINISM*

A Report of Six Cases

ALEXANDER MARBLE, M.D.,† AND LELAND S. MCKITTRICK, M.D.‡

BOSTON

ALTHOUGH in recent years many publications regarding patients with pancreatic islet-cell tumors have appeared, the condition is sufficiently frequent to make additional reports desirable. Since 1938 we have observed 6 patients in whom the diagnosis was verified at operation performed by one of us (L. S. McK.). Our experience with these patients forms the basis for the present paper. This report is particularly worth while at the present time because it provides a four-year to seven-year postoperative follow-up study of the patients concerned. In 5 of the 6 cases removal of a single adenoma at operation resulted in relief of symptoms that has persisted to date. In 1 case death followed a few weeks after operation, which disclosed an islet-cell carcinoma with multiple metastases in the liver. A summary of the data in these cases is given in Table 1.

CASE REPORTS

CASE 1. P. F., a 16-year-old girl was first seen on November 28, 1938. She had been well until the summer of 1933, when she began to have occasional spells of stupor that progressed into definite unconsciousness. In July of that year she was seen in the outpatient department of a children's hospital and in the next month at another hospital, where, while waiting for an examination after having missed the noonday meal, she fainted, remaining unconscious for about an hour, during this period she had a few convulsive twitchings of the shoulders and face and voided involuntarily. She was admitted for observation to the hospital, where she remained from August 18 to September 14. The fasting blood-sugar concentration was consistently low (of twelve determinations, ten were below 60 mg. per 100 cc., including five that were below 50 mg.). An attack of coma brought on by starvation was relieved by the intravenous injection of glucose, consequently the diagnosis of hyperinsulinism was made, and the patient discharged with instructions regarding diet. She was readmitted on January 8, 1934, because in the week before entry attacks had occurred far more frequently than

previously. During this admission, after extensive studies, abdominal exploration was carried out. No tumor was found, a small section of the tail of the pancreas removed for histologic examination was found to consist of normal tissue. The postoperative course was uneventful, and the patient was discharged on February 27 with instructions to follow a diet restricted in carbohydrate. The patient was subsequently seen in the Out-Patient Department on only one occasion, on March 16, 1934, when she reported that she had had no attacks since discharge from the hospital.

The patient was free from obvious attacks until August, 1938, when she suffered a recurrence of spells of drowsiness and weakness, particularly after an overnight fast. These symptoms were relieved by food or glucose. The attacks increased in frequency, and on November 8 she was taken to a third hospital in a deep stupor. On admission the blood-sugar concentration was 38 mg. per 100 cc. The patient was revived from her stuporous condition by means of concentrated glucose intravenously and sweetened orange juice orally. During a stay of 16 days in the hospital she was kept from hypoglycemia by frequent feedings. Roentgenograms of the chest, skull and abdomen gave normal findings, films of the teeth showed evidence of considerable infection. Electroencephalograms were thought to suggest that the patient, in addition to the overactivity of the sugar-disposing mechanism, had an epileptoid condition of cerebral dysrhythmia.

The patient was admitted to the New England Deaconess Hospital for further study on January 3, 1939. In the preceding days occasional attacks of hypoglycemia had continued. She had taken a bedtime lunch routinely, as well as orange juice at 5:00 o'clock each morning. Physical examination showed a small thin, underdeveloped girl who seemed pale and listless. The body weight was 107 pounds (48.6 kg.) and the height 4 feet 9½ inches (147 cm.). The teeth were poor, there was marked caries despite the extraction of 5 teeth a few days previously. The heart was normal in size and regular in rhythm and over the whole precordium a prominent systolic murmur was audible. The abdomen was normal, there was a long healed operative scar in the left upper abdomen. The blood pressure was 104/70.

Questioning revealed that there had been no significant illnesses before 1933 and no abnormality except that discussed above. The father, mother, a brother and two sisters were living and well.

After 8:00 o'clock on the morning following admission the patient became increasingly drowsy so that by the time breakfast was served—45 minutes later—she was unconscious. The blood-sugar concentration was 28 mg. per 100 cc. The administration of glucose intravenously brought about prompt relief. During the next 2 weeks the patient was kept on a diet that included from 199 to 315 gm. of carbohydrate daily. By means of feedings between meals she was kept from hypoglycemic attacks.

The results of the glucose-tolerance tests in this case—and in the other 5 cases of the series—are shown in Table 2.

Examination of the urine showed no albumin, bile, diacetic acid or sugar, and examination of the sediment was nega-

*From the George F. Baker Clinic (Elliott P. Joslin, M.D., medical director), New England Deaconess Hospital and the West Surgical Service, Massachusetts General Hospital.

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‡Associate in surgery, Harvard Medical School, surgeon-in-chief, Palmer Memorial Hospital, visiting surgeon, Massachusetts General Hospital.

*A detailed account of the early history studies and findings at the first operation in this case was presented by Boone¹ in 1934.

tive Examination of the blood revealed a red-cell count of 4,660,000, with a hemoglobin of 82 per cent (Sahl), and a white-cell count of 10,150, the blood smear was essentially normal. The blood Hinton reaction was negative. The cholesterol content of the blood plasma was 163 mg per 100 cc. The bromsulfalein test of liver function gave normal results. Roentgenograms of the skull and chest and of the region of the kidneys, ureters and bladder were normal. A gastrointestinal series was likewise normal, there was no change in the size and shape of the duodenal loop.

In view of the exacerbation of hypoglycemic attacks, it was thought justifiable to carry out a second pancreatic exploration despite the negative findings 5 years previously. Consequently, on January 16, exploration was performed under ether anesthesia through a long, curved transverse incision just above the umbilicus through both rectus muscles of the type used by Whipple.³ Because of adhesions that had obliterated the lesser peritoneal cavity, painstaking dissection was necessary to free the stomach from the pancreas. The entire anterior aspect of the pancreas was exposed, from the extreme tip of the tail to the portion of the head that was visible anteriorly, the body and tail were then completely freed posteriorly. Inspection and careful palpation revealed no tumor in the part of the pancreas thus exposed. Attention was next directed to the remainder of the head of the pancreas. The entire head, together with the loop of duodenum, was elevated as much as the important vascular structures permitted. With the thumb and fingers of the examiner grasping the head of the pancreas, it was possible to feel a small tumor completely within pancreatic tissue. An exploratory incision brought into view a somewhat lobulated, encapsulated, reddish-purple nodule, which was completely removed, the rest of the organ was again palpated for other tumors, none being found.

The following was the description of the nodule by the pathologist:

The tumor was a delicately encapsulated, reddish-brown, moderately yielding nodule, almost spherical, measuring 1.2 by 1.1 by 0.9 cm. On cross section it was found to be soft, moist, pale and reddish brown, with a few fine, gray foci indefinitely marked. Microscopic examination showed adenomatous tissue made up of beta cells.

The postoperative course was uneventful. Blood-sugar values during the first 48 hours ranged from 120 to 310 mg per 100 cc, but during most of this time the patient was receiving glucose solution intravenously. From the 2nd postoperative day on, all random blood-sugar values were uniformly normal. Electroencephalograms taken after operation were normal. The patient was discharged from the hospital on February 4, in good condition.

On assays for insulin content the tissue was found to contain approximately 7 units of insulin per gram, or about twice the amount present in normal pancreatic tissue.*

After operation the patient continued in good condition. There were no attacks suggesting hypoglycemia, random blood-sugar values were normal and glucose-tolerance tests showed a normal response. The blood-sugar concentration on May 18, 1946, after an overnight fast, was 84 mg per 100 cc. When last heard from in August, 1946, over 7 years after operation, the patient had continued to feel well.

CASE 2 L. H., a 49-year-old woman, was first seen on June 20, 1939. She had been well until January, 1931, when she began experiencing attacks of extreme weakness and drowsiness. During such periods she was unable to speak, felt listless and complained that the hands were cold and numb.

Examination revealed no satisfactory cause of the difficulty, but the patient seemed to improve on a high-carbohydrate diet, with frequent feedings, during spells of weakness she obtained relief by drinking orange juice. With the added food she gained in weight from 165 pounds in 1931 to 214 pounds in 1934. In May, 1934, the spells became severer. The patient was admitted to a hospital, where blood-sugar values as low as 42 mg per 100 cc were found. A glucose-tolerance test carried out for 4 hours was reported to be entirely normal. She progressed fairly well until November, 1938, when she was readmitted to the hospital with the same complaints. The weight at that time was 220 pounds, and the patient stated that for the preceding 4 years she had had

one or two attacks a week, which were relieved by orange juice. A glucose-tolerance test carried out on November 1 showed the blood-sugar concentration after fasting to be 59 mg per 100 cc, following the administration of 170 gm. glucose the value after the 1st hour was 183 mg, after the 2nd hour 155 mg and after the 3rd hour 133 mg per 100 cc. During the hospital stay in November the amount of carbohydrate in the diet was varied from 60 to 225 gm daily, with no significant change in the condition except a loss in weight to 187 pounds.

The patient was admitted to the New England Deaconess Hospital on June 20, 1939. Physical examination showed an obese woman, the body weight was 186 pounds (84.5 kg.) and the height 63 inches (161 cm). The heart was normal in size and regular in rhythm, and a moderately loud systolic murmur could be heard over the precordium. The lungs were clear, the abdomen normal, and the blood pressure 144/82. Examination of the blood revealed a red-cell count of 4,740,000, with a hemoglobin of 77 per cent (Sahl), and a white-cell count of 14,000, with a normal blood smear except for slight acromia. Examination of the urine showed 10 mg of albumin per 100 cc, no sugar, diacetic acid or bile and a normal sediment. The bromsulfalein test of liver function gave normal results, and the blood bilirubin was 0.2 mg per 100 cc. The basal metabolic rate was -10 per cent. A blood Hinton test was negative.

The past history was essentially noncontributory. The family history was irrelevant, the patient had three grown children — one son and two daughters — living and well.

During the first 9 days in the hospital the patient appeared generally dazed, with slow reactions. Blood-sugar values as low as 31 mg per 100 cc were found. Roentgenograms of the skull were normal, as was a gastrointestinal series, in which the duodenal sweep seemed of normal extent.

Exploratory laparotomy was carried out on June 28, under ether anesthesia, through a transverse incision. The pancreas was easily exposed and freed from its attachment without difficulty, disclosing a small nodule at about the midportion of the organ on the anterior aspect near the lower border. Incision showed it to be a soft, friable, purplish tumor that on section was found to include considerable grayish necrotic material. The tumor was well encapsulated and could be completely removed, although because of its friability, during the removal it broke into two parts, the larger of which was 8 mm in diameter. Careful inspection and palpation failed to disclose any other tumors. Microscopic examination showed the nodule removed to be an islet-cell adenoma made up chiefly of beta cells. Assay showed the tumor to contain more than 100 units of insulin per gram.

The postoperative course was uneventful, and the patient left the hospital in good condition on July 20. Except for fasting blood-sugar values of 130 mg and 120 mg per 100 cc, for the 1st and 2nd days respectively after operation, all values postoperatively were normal and the patient was entirely free from hypoglycemic attacks. A glucose-tolerance test carried out on July 18 gave entirely normal results (Table 2).

The patient reported for examination on October 18, 1939. May 21, 1940, and May 29, 1942, when questioning revealed no symptoms suggesting hypoglycemia and careful study, including glucose-tolerance tests, yielded results within normal limits except that, in general, blood-sugar values 4, 5 and 6 hours after the administration of glucose tended to be and 6 hours after the administration of glucose tended to be subnormal or toward the lower limit of normal. The patient remained entirely asymptomatic, however, and blood-sugar values after an overnight fast were normal. In the last letter received from her, dated August 4, 1946, she stated that she had been well and active.

CASE 3 F. P. H., a 58-year-old woman when first seen on September 15, 1938, had been well until June, 1935, when she had had an attack of fainting followed subsequently by periods of coma during which she slept 12 to 48 hours. At times she suffered blankness of vision. In 1936, adopting a suggestion from a newspaper article, she began to take sugar for the attacks and found that this gave relief. The periods of drowsiness, mental confusion and speech disturbance continued, however. The patient first consulted a physician on October, 1937, when fainting spells were occurring once or twice daily and often on awakening at about 5:00 a.m. She entered a hospital on June 23, 1938. The fasting blood sugar,

*All assays in these cases were performed by Mr. George B. Walden, of the Research Laboratories of Eli Lilly and Company Indianapolis to whom frozen portions of the tumors were sent.

†Previously reported in part by Gray.⁴

was 27 mg per 100 cc 2 days later, was subsequently to average about 45 mg. The patient was put on a low-hydrate, low-protein, high-fat diet, on which she did well for a time, but returned later because of recurrence of symptoms and the need of increasing the feedings to every 3 hours to prevent attacks. A diagnosis of probable cell tumor was made.

During the first admission to the New England Deaconess Hospital in September, 1938, studies confirmed this diagnosis. Fasting blood-sugar values as low as 30 mg per 100 cc obtained, and on one occasion, after exercise, a value of 1 mg was reported. Roentgenograms of the heart, lungs, and gastrointestinal tract were normal. Examination of ocular fundi gave normal findings. The basal metabolic rate was -7 per cent. The blood calcium was 10.1 mg and blood phosphorus 3.8 mg per 100 cc. The bromsulfalein of liver function gave normal results. An electrocardiogram was essentially normal. The blood Hinton reaction was negative.

Her past and family histories were irrelevant. Review of x-rays revealed nothing of consequence except for "nervousness" and for exertional dyspnea noted since a gain in weight. Physical examination showed an obese, healthy-appearing woman. The body weight was 188 pounds (85.5 kg), and height was 63 inches (161 cm). Examination of the heart, lungs and abdomen was essentially negative, and the blood pressure varied from 115/65 to 160/80.

Abdominal exploration was advised but was refused by the patient. Although she promised to return soon for operation, actually she did not re-enter the hospital until September 12, 1939. Within a month or so following discharge in 1938, she had fallen at home, suffering injuries that kept her bed for 28 weeks. The hypoglycemic attacks had continued during the year and had been particularly frequent and marked after resumption of physical activity. Unless food was taken about every 3 hours, vision became blurred and mental dullness, stupor, unconsciousness and, at times, convulsions followed. During the 2 weeks prior to the second admission a special nurse had been in attendance in the home and had awakened the patient every 2½ hours for feedings during the night.

Physical examination showed the patient to be even more obese than at the former visit—205 pounds (92.3 kg), as compared with 188 pounds (85.5 kg) a year previously. The heart seemed normal in size and was regular in rhythm, a slight generalized systolic murmur could be heard. The lungs were clear, and the abdomen normal to palpation. The fasting blood sugar on the morning after admission was 29 mg per 100 cc. Examination of the blood showed a red-cell count of 4,540,000, with a hemoglobin of 86 per cent (Sahli), and a white-cell count of 12,700, with a normal differential. The urine contained a trace of sugar but no albumin, bile or acetic acid, and the sediment was essentially normal. The food nonprotein nitrogen was 31 mg, and the cholesterol content of the blood plasma 153 mg per 100 cc (the free cholesterol was 35 mg per 100 cc).

It was soon evident that unusual precautions were essential to keep the patient from becoming hypoglycemic. The blood-sugar values were so low and the attacks were so frequent, despite careful supervision, that early exploratory operation was carried out 4 days after admission. A transverse incision was made, and the pancreas exposed through the gastrotomy omentum. After mobilization of the organ a tumor about 1.5 to 2.0 cm in diameter was visible toward the tip of the head of the pancreas, which was adherent to adjacent structures, lay high and was accessible only with great difficulty. Finally it was freed, and resection of the tip of the organ was carried out, although not more than 3.0 to 3.5 cm of the pancreas was removed. The tumor was firm and seemed to infiltrate surrounding tissue, suggesting a malignant process. The liver was studded with grayish-white nodules varying in diameter from several millimeters to about 2 cm. A wedge from one of these nodules was excised and examined.

The postoperative course was extraordinary. For the 1st week blood-sugar values were within normal limits. Then on September 23, a week after operation, small amounts of sugar appeared in the urine, and a capillary blood-sugar value at 11:00 a.m. was 200 mg per 100 cc. In the next 3 days glycosuria and glycemia increased, so that urine tests for sugar by the Benedict method ranged from yellow to red, and the fasting blood sugar on September 27 was 247 mg per 100 cc.

Consequently, treatment with protamine-zinc insulin was instituted and continued for a total of 29 days in a dosage of 12 to 16 units daily before breakfast. The food intake during this period was variable because of the patient's condition, the amount of carbohydrate taken daily averaged 149 gm, that of protein 41 gm and that of fat 35 gm. On this regime, fasting blood-sugar values varied from 120 to 150 mg per 100 cc. From October 25 until the patient's death on November 3 no insulin was used.

In the few days immediately following operation the patient's general condition was much improved. Then, however, crepitant rales were heard at the lung bases, silant rales were heard throughout the chest, and moderate fever was present. Roentgenograms showed patches of bronchopneumonia in the lower half of both lung fields. From the day of operation, September 16, until September 19, the patient received a constant infusion of glucose into a vein at the elbow of the right arm. An area of induration and tenderness developed above the antecubital space on the outer aspect of the arm, the inflammation gradually subsided but healing never entirely took place, and on October 21 the right arm was more swollen than before. At that time generalized anasarca also developed. The right external jugular vein became palpable and tender. The clinical impression was that the swelling of the right arm did not represent an infection, but rather edema secondary to venous thrombosis. Later however, a hard, slightly tender area about 5 cm in diameter developed in the right lower axilla, on October 10 this was incised, allowing 60 to 90 cc of thick pus to drain.

Immediately after the abdominal operation the body temperature rose to a maximum of 103°F and then ranged between 99 and 101°F for 4 or 5 weeks before completely subsiding. The operative wound in the abdomen healed readily except for a portion on the left side where a sinus persisted, during the 2nd, 3rd and 4th weeks after operation, large quantities of creamy yellow pus drained from this wound. During that time there were nausea and upper abdominal pain made worse by eating, so that for a considerable period the patient was maintained on glucose given subcutaneously. During the last 2 weeks of life the amount of drainage from the operative wound subsided.

Throughout the postoperative course and, indeed, before operation the breathing was rapid somewhat labored and wheezing in type. By October 28, however, the patient seemed better in almost every way and the breathing was easier and quieter. On November 2 she was allowed up in a chair for a short period. On November 3, after she had been up about 30 minutes and was ready to return to bed she developed an acute attack of shortness of breath and quickly became comatose, pulseless and cyanotic. She rapidly failed and died within a few minutes.

Autopsy. At post-mortem examination no evidence of residual tumor was found in the pancreas. The liver was studded with many firm white, glistening, well demarcated nodules varying from 2 to 3 cm in diameter. The tumor replaced one third to half the liver substance. Histologic examination of the tumor tissue previously removed from the pancreas and liver at operation, and of that obtained from the liver at autopsy, showed the growth to be an islet-cell carcinoma of mixed type. Beta cells were demonstrated in the primary tumor but not in the metastatic lesions. Microscopic examination of the pituitary gland revealed marked basophilism. In addition to these findings, autopsy disclosed extensive thrombophlebitis of the right brachial, right axillary, right subclavian and right internal jugular veins, with complete occlusion of these vessels. There was thrombosis of the superior vena cava, with partial organization and occlusion. The immediate cause of death was pulmonary embolism, there were emboli in most of the secondary ramifications of the pulmonary artery. There were recent and old infarcts in the lower lobe of the right lung. (Detailed autopsy findings in this case, together with photomicrographs, appear in the article by Gray.)

Attempts in the laboratory of the New England Deaconess Hospital to determine the insulin content both of the primary tumor and of the nodules were unsuccessful from a quantitative standpoint probably because of unfamiliarity with the technique. A moderate lowering of the blood sugar was obtained, however, in a rabbit following the injection of an extract of liver nodules.

CASE 4 * B M, a 29-year-old housewife, was seen in the Out Patient Department of the Massachusetts General Hospital on August 14, 1940, and was admitted as an inpatient on September 12. She had been well up until December, 1937, when she began to experience attacks of weakness, dizziness, faintness and sweating and a feeling as if her mind were "paralyzed." At 11 00 a.m. on December 24, while at work at her sewing machine, she began to perspire profusely, her mind became blank and she fainted, unconsciousness lasted 17 hours. After this episode she gave up her job and remained at home for 5 months. She then resumed work, but after 4 or 5 weeks had another fainting spell while at work, on this occasion she was unconscious for 18 hours. Following another attack 2 days later, she was admitted to a hospital, where the blood sugar was found to be only 35 mg per 100 cc and roentgenograms of the skull were said to show no sign of tumor. She was placed on a special diet but found that to keep comfortable she always had to eat more than prescribed, and she had adopted a regime of eating between meals and at bedtime, in addition to the regular three meals. She had gained 40 pounds in weight in 2½ years. Although with such treatment she felt better and gained weight and strength and the attacks of syncope became milder, they seemed to occur almost as frequently as before (three or four times a month)—more frequently at the time of the menstrual period. The patient stated that during attacks she seemed unable to complete an action already started. The attacks were always relieved or aborted by food or glucose, and later the patient could recall nothing regarding the attack and chills and a "frozen feeling" were often present for some time.

A review of the past history showed no important illnesses, the patient remembered only measles and influenza in childhood. The family history was irrelevant except that two paternal aunts had died of cancer. The patient had been married for five years and had one child 3 years old.

Physical examination showed no significant abnormalities. The upper teeth were replaced by a satisfactory denture. The blood pressure was 118/85. The body weight was 124 pounds (56.5 kg) and the height 61½ inches (156 cm).

On August 14, 17 and 21 the fasting blood-sugar values were 38, 35 and 41 mg per 100 cc, respectively, and on September 13, 14, 27 and 30, they were 26, 30, 25 and 40 mg, respectively. Examination of the blood revealed a red-cell count of 4,940,000, with a hemoglobin of 90 per cent, and a white-cell count of 10,500, with a normal differential. The urine contained no albumin, sugar, bile or diacetic acid, and the sediment was normal. A blood Wassermann test was negative. The serum chloride was 99.6 and 108.1 milliequiv per liter on two occasions. The blood cholesterol was 144 mg, the serum nonprotein nitrogen 24 mg, and the serum protein 7.0 gm per 100 cc. The basal metabolic rate was -6 per cent. Roentgenograms of the gastrointestinal tract, chest and skull were negative.

On October 7 exploratory laparotomy was carried out through a wide transverse incision under nitrous oxide, oxygen and ether anesthesia. Considerable difficulty was experienced in locating a tumor, and even more trouble in removing it. It was finally found in and removed from the substance of the head of the pancreas, after removal, the tumor was found to have been directly over the beginning of the portal vein, which was not damaged during the operation. The tumor was definitely encapsulated and was soft, friable and purplish. During removal it was broken up into small fragments, the total weight was 750 mg. Assay showed a normal insulin content (3 units per gram). Histologically the tumor was an islet-cell adenoma.

The postoperative course was uneventful. The fasting blood sugar, which on the morning of October 8 was 155 mg per 100 cc, was 127 mg on October 9 and 93 mg on October 11. Following this the blood sugar stabilized at an entirely normal level and continued so until discharge on October 28.

The patient was seen in the Out Patient Department of the Massachusetts General Hospital on December 20, about 2½ months after operation. She had had no spells of weakness or fainting, although the appetite continued to be extraordinarily good. At this visit a blood-sugar determination about 12 hours after a meal was 67 mg per 100 cc, another determination, made 2 hours later and still in the fasting state, was 76 mg per 100 cc. At a visit on July 2, 1941, the

blood sugar 4 hours after eating a sandwich and milk was 97 mg per 100 cc. The patient had continued to feel entirely well and weighed 118 pounds. She was last seen on January 3, 1944, when the fasting blood sugar was 102 mg per 100 cc. In a letter dated April 26, 1946, she stated that she was doing all the housework for her family of five and that her appetite, weight and energy were normal.

CASE 5 E R, a 32-year-old bartender and taxi driver, had been admitted to a hospital on October 1, 1940, with the complaint that for a year he had experienced attacks of twitching of the face and neck, staggering in gait, weakness, dizziness and sleepiness, all relieved by food. Blood-sugar studies had shown extremely low values, and the diagnosis of probable islet-cell tumor was made. At operation on October 15 no tumor could be felt in the pancreas. The blood-sugar values continued to be low, and attacks persisted despite a high-protein, low-carbohydrate diet and phenobarbital daily.

Questioning on admission to the New England Deaconess Hospital on October 23, 1941, revealed that the symptoms had included the following: drowsiness leading to unconsciousness, weakness, sweating, rapid heart action, trembling and nervousness, numbness especially about the lips, inability to concentrate or to think clearly, staggering gait as that of a drunken man, twitching of the hands and face, peevishness, aggressiveness and blurring of vision. The first symptom usually noted was drowsiness. Attacks were definitely brought on more easily by exercise and by prolonged abstinence from food, food gave almost immediate relief. The patient first noticed his trouble because of difficulty at times in tying his tie. As a bartender he got along fairly well, because he could usually forestall attacks by taking food, but even so, at times he confused orders. Once while a taxi driver, he pulled his car up to the curb, got out and walked aimlessly for 5 blocks before a friend saw that something was wrong and took care of him, afterward, the patient did not recall the incident.

Physical examination showed no abnormalities. The patient seemed well developed and well nourished, the blood pressure was 104/70. The body weight was 166½ pounds (75.8 kg). Examination of the ocular fundi gave normal findings. Examination of the blood revealed a red-cell count of 5,070,000, with a hemoglobin of 17.7 gm per 100 cc, and a white-cell count of 10,650, with a normal differential. The urine contained no albumin, sugar, bile or diacetic acid, and examination of the sediment was negative. The serum protein was 6.4 gm and the nonprotein nitrogen 30 mg per 100 cc, and the serum chloride 97.3 milliequiv per liter. Roentgenograms of the skull, chest and gastrointestinal tract were negative. An electrocardiogram was normal.

At exploratory laparotomy on October 30 a completely encapsulated, soft tumor measuring 1.5 by 1.5 by 1.7 cm was removed from the pancreas. The tumor was a mottled red-gray in color. On microscopic examination it proved to be an adenoma of insular origin, consisting chiefly of beta cells, with scattered foci of ductal epithelium. Under sterile conditions Dr. J. Herbert Waite transplanted a small section of the tumor into the anterior chamber of the eye of a normal rabbit, the tumor failed to develop, however, and no signs of excessive insulin activity were evident from periodic tests of the rabbit's blood sugar.

Following operation the patient developed bronchopneumonia at both lung bases, particularly the left. Consequently he was uncomfortable during the first several days after operation, but gradually improved and left the hospital on December 1 in good condition. From his home physician it was learned that as late as May, 1946, he had continued to feel well and had had no attacks suggesting hypoglycemia.

CASE 6 S F, a 45-year-old farmer, was admitted to the New England Deaconess Hospital on November 8, 1941. He had felt well until 2 years previously, when he began to notice dizziness brought on particularly by exercise and was relieved by eating. Symptoms gradually increased to include weakness, fatigue and at times a change in temperament, irritability and a feeling of mental confusion. Various types of medical treatment had proved ineffective. The first indication of difficulty had occurred in the spring of 1938 while the patient was plowing corn. He noticed increasing difficulty and finally, when he stopped and let go of the reins, which had been partly supporting him, he felt dizzy and sank to

*This case was reported in 1941.⁵ Permission to include the patient in the present series was given by the Executive Committee of the Massachusetts General Hospital.

ground. When he finally got to the house and obtained relief, he felt relieved at once. This episode was the beginning of a long series of similar experiences. He soon adopted a schedule of taking orange juice or other food as soon as he awoke in the morning, before starting work. During the last several months he had had to give up most of the work about the farm because of the danger of hypoglycemic attacks. He regularly between meals and carried sugar in his pocket at all times. When attempts were made to arouse him from hypoglycemic stupor, he was occasionally simply confused and co-operated with difficulty, at other times he was pugnacious.

The family and past histories, except as already stated, are irrelevant.

Physical examination showed a well developed and well nourished man. The body weight was 208 pounds (94.5 kg). The heart, lungs and abdomen were normal, and the blood pressure was 110/70.

Examination of the blood showed a red-cell count of 3,200,000, with a hemoglobin of 15 mg per 100 cc, and a white-cell count of 9,600, with a normal differential. The urine contained only a slight trace of albumin and no sugar, and no diacetic acid; examination of the sediment was essentially negative. The blood sugar on November 10 was 41 mg per 100 cc. Subsequent values were uniformly at a low level, usually below 50 mg per 100 cc.

Operation was carried out on November 18 under nitrous oxide, oxygen and ether anesthesia. A long transverse incision was made across both rectus muscles. Exposure of the pancreas was quite difficult. The capsule was incised along the lower margin, and the pancreas lifted from its bed so that it could be carefully palpated between the fingers from the tip of the tail to the junction of the superior mesenteric and splenic veins. The free margin of the duodenum was then mobilized so that the head of the pancreas could be palpated between the fingers, the exploration being carried up to the point at which the pancreas had been explored from the other approach. Throughout this procedure nothing abnormal was seen or felt except that at the free margin of the head in the duodenal loop, there was a small, firm area about 1 cm in diameter within the pancreatic tissue. Although this area did not seem unusual, in the absence of any other abnormality, it seemed necessary to explore it further. This proved difficult, because of the extreme vascularity of the region. By blunt dissection a deep, purplish, encapsulated tumor about 1 cm in its greatest diameter was removed in one piece. Histologic examination showed an adenoma of the islet cells, with hyalinized stroma.

The postoperative course was uneventful. No further hypoglycemic attacks were experienced, and the blood-sugar values were within the normal range. The patient continued to be well. On August 4, 1946 (almost 5 years after operation), the patient stated in a letter that he had been in excellent health and had had no further difficulty of the sort experienced prior to the operation.

DISCUSSION

The 6 cases reported above are instructive in that they illustrate the various problems encountered in the diagnosis and treatment of patients with hyperinsulinism. Of especial interest are the patients in Cases 1 and 5, in whom no tumor had been found at a previous operation elsewhere, and the patient in Case 3, who was found to have a malignant tumor with metastases in the liver.

Symptomatology

Although the symptoms experienced by the patients were those common to reactions due to an overdose of insulin, in general they lacked the acute nature encountered following unmodified insulin. Although these patients often experienced sweating and nervousness, the symptoms were usually increasing mental confusion, bizarre behavior and drowsiness that finally passed into total uncon-

sciousness, with or without convulsions. Such symptoms developed if food was withheld for more than a few hours, and an overnight fast invariably resulted in a blood-sugar level well below normal and usually below 50 mg per 100 cc. In all cases physical exercise depressed the blood-sugar level still further and increased and hastened the onset of symptoms. Food or glucose gave prompt relief.

Diagnosis

Our experience with these and with other patients in whom the possibility of an islet-cell tumor has been raised is in agreement with that of Whipple³ and leads to the belief that when marked hypoglycemia with blood-sugar values below 50 mg per 100 cc regularly develops on fasting and is relieved by food, the presence of an islet-cell tumor must be assumed until proved otherwise, provided that by careful study extrapancreatic causes for the hypoglycemia have been excluded. These include diseases of the liver affecting glycogen storage and conditions associated with hypofunctioning of the adrenal cortex, the anterior lobe of the pituitary gland and the thyroid gland. Since conclusive evidence is lacking that the post-prandial hypoglycemia sometimes described in patients suffering from chronic fatigue⁶ is due to excessive nervous stimulation of islet tissue, the term "hypoglycemia" rather than "hyperinsulinism" is to be preferred for this condition.

No elaborate diagnostic procedures are necessary. The characteristic symptoms associated with well marked hypoglycemia brought on by fasting, increased by physical exertion and relieved by food are the important features. As an aid in the diagnosis, the glucose-tolerance test is of value only if carried out for a sufficient length of time — that is for four to six hours. Characteristically, the fasting blood sugar starts at a low level — usually below 50 and frequently below 40 mg per 100 cc. Following the administration of glucose, the rise in the blood sugar may be within normal limits or the curve may be diabetic in type. Conn and Conn⁷ suggest that the type of curve depends on the amount of carbohydrate in the diet of the preceding few days, diets high in carbohydrate increase and those low in carbohydrate reduce sugar tolerance. The glucose-tolerance curve up to the third hour, therefore, may be essentially normal or mildly diabetic in type except for the initial value. After three hours, however, the blood sugar usually falls sharply to a low level (in 5 of the 6 cases reported above to approximately 40 mg per 100 cc) and in the fourth, fifth and sixth hours shows no tendency to rise spontaneously (Table 2). This last fact is significant in normal persons one often obtains a hypoglycemic phase in the glucose-tolerance test but, presumably owing to the compensatory secretion of adrenaline, there is a spontaneous return to normal values. Such a return does not occur in

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TABLE 1 Data and Results of Treatment in 6 Cases of Pancreatic Islet-Cell Tumor

CASE No	SEX	AGE AT ONSET OF SYMPTOMS	AGE AT OPERATION	LOWEST FASTING BLOOD SUGAR	DATE OF OPERATION	LOCATION OF TUMOR	SIZE OF TUMOR	TYPE OF TUMOR	INSULIN CONTENT OF TUMOR	ENCAPSULATION OF TUMOR	BLOOD VESSEL INVASION	METASTASIS	RESULT OF TREATMENT (1946)
1	F	37	37	mg/100 cc 28	1/16/39	Head of pancreas	12 x 11 x 9 mm	Adenoma	More than 100 units/gm	Incomplete	None	—	Patient asymptomatic free
2	F	41	49	28	6/28/39	Body of pancreas	15 (diameter)	Adenoma	—	Specimen unsatisfactory for examination	None	—	Patient asymptomatic free
3	F	55	59	21	9/16/39	Tail of pancreas	18 x 18 x 13	Carcinoma (mixed-cell type)	—	Incomplete	Present	Multiple nodules in liver	Death on November 3, 1939
4	F	26	29	25	10/7/40	Head of pancreas	—	Adenoma	3	Incomplete	None	—	Patient asymptomatic free
5	M	30	32	33	10/31/41	Head of pancreas	15 x 15 x 17	Adenoma	100	Incomplete	None	—	Patient asymptomatic free
6	M	43	45	48	11/18/41	Head of pancreas	10 (diameter)	Adenoma	—	Incomplete	Questionable	—	Patient asymptomatic free

TABLE 3 Capillary Blood-Sugar Levels after Subcutaneous Injection of Various Drugs Prior to Operation

CASE No	DATE	DRUG ADMINISTERED			CONCENTRATION BEFORE INJECTION		CONCENTRATION AFTER INJECTION OF DRUG									
		LUPULURINE (1:1000)	PITUITARY EXTRACT*	UNMODIFIED INSULIN	PROTAMINE TARTARATE (1:2000)	mg/100 cc	mg/100 cc	1/2 hr	1 hr	1 1/2 hr	2 hr	3 hr	4 hr	5 hr	6 hr	7 hr
1	1/11/39	0.5				48	82	85	77	66	55	50	48	44		
	1/12/39			2.0		50	103	103	107	101	109	108	108	104		
	1/13/39		0.5			66	151	50	51	50	—	—	—	—		
	2/11/39†				0.2	138	127	114	101	101	—	—	—	—		
	2/12/39†	0.5			0.4	197	147	168	192	199	205	204	177	160		
	2/13/39†					63	67	68	67	68	69	65	65	64		
	2/14/39†			6.6		99	—	89	—	75	—	75	70	66		
	6/20/39					47	49	49	49	40	46	—	—	—		
	6/24/39	1.0	1.0†			50	50	50	49	55	61	63	69	67		
	9/21/38	1.0				39	45	50	56	50	42	—	—	—		
5	10/30/41	0.5				53	55	66	69	67	66	65	—	—		
	10/30/41			7.0		89	82	77	56	53	47	46	—	—		
6§	11/13/41			8.0		45	—	—	—	35	—	32	—	35		

*Surgical double strength extract was used (1 cc = 20 i u.)

†After operation

‡Extract was injected intramuscularly

§Venous blood was employed in the determination

hyperinsulinism, probably because of the continuous secretion of insulin by the islet-cell tumor

The glucose-tolerance curve in patients with hyperinsulinism differs from that described by Portis⁶ in patients with hypoglycemia associated with vagotonia and fatigue in the following particulars in the latter condition the fasting blood sugar, although perhaps lower than the average normal, is not depressed to the extent seen in hyperinsulinism, the

In 5 of the patients the tumor was an adenoma, more or less encapsulated, composed chiefly of beta cells. In 1 a carcinoma of mixed-cell type was present, with multiple metastatic nodules in the liver.

The tumors in the 6 patients were uniformly small nodules, varying from about 1 to 2 cm in diameter, although in the patient with carcinoma several of the nodules in the liver were larger. Although most of the reported islet-cell tumors were small, average

TABLE 2 Blood-Sugar Levels after Oral Administration of 100 gm of Glucose

CASE No	DATE OF TEST	CONCENTRATION BEFORE TEST	CONCENTRATION AFTER ADMINISTRATION OF GLUCOSE						
			1/2 HR.	1 HR.	2 HR.	3 HR.	4 HR.	5 HR.	6 HR.
			mg /100 cc	mg /100 cc	mg /100 cc	mg /100 cc	mg /100 cc	mg /100 cc	mg /100 cc
1	1/ 7/39	69	161	136	112	67	54	52	—
		54*	137	105	73	50	56	43	—
	1/14/39	45	100	206	238	102	80	46	48
	2/10/39†	95	188	150	132	—	110	81	92
2	6/ 1/39	95	214	180	110	122	87	90	95
	6/22/39	36	121	102	80	—	40	38	39
		66	147	123	103	70	61	60	56
	7/18/39	—	140	140	120	100	50	70	—
	10/18/39	110	160	100	140	100	90	80	100
		89	130	118	77	—	56	—	75
		106	164	146	111	123	97	75	97
	5/22/40	90	115	100	73	54	66	72	81
3	5/30/42	74	133	69	74	69	59	57	—
	9/19/38	34	106	138	126	104	49	35	—
		35	135	157	138	115	55	35	—
	9/14/39	28	67	82	104	80	45	—	—
4		34	95	112	127	90	44	—	—
	9/27/40	25	92	166	208	196	100	72	47
	10/21/40	83	112	123	127	128	—	—	—
	10/23/40	—	96	110	135	—	111	102	96
5	10/15/40‡	35	123	110	100	87	58	51	—
	5/ 2/41	62	—	169	148	100	52	39	—
	7/11/41†	43	123	160	170	138	80	73	—
	11/26/41	93	153	141	120	88	76	73	—
6		95	190	202	155	112	95	73	—
	11/14/41	—	118	166	134	115	68	57	—
		65	133	190	156	132	75	59	—
	12/ 5/41	78	137	—	106	78	63	84	—

*Figures in italics represent values obtained on capillary blood, the unitalicized figures representing those obtained on venous blood

†On this date 80 gm of glucose was given

‡Tests performed at Duval County Hospital, Jacksonville, Florida

curve tends to be flat, and the lowest blood sugar usually occurs two, three or four hours after the administration of glucose, and there is a tendency to return to normal without the administration of food or glucose

Various secondary tests may be carried out, including blood-sugar studies following the giving of epinephrine, pituitary extract, ergotamine and insulin. One would expect the blood-sugar-raising effect of epinephrine and pituitary extract to be less and the blood-sugar-lowering effect of insulin to be greater than those in normal persons studied under the same conditions. This is true in general, but our experience has been that although the results obtained are interesting, they are apt to be variable and do not contribute significantly to the diagnosis. Table 3 shows the values obtained in such studies with our patients.

Location, Type and Size of Tumors

Although islet-cell tumors are said to occur most frequently in the tail of the pancreas, in these 6 cases the tumor was found in the head in 4 cases and once each in the body and tail of the pancreas

ing about 1.5 cm in diameter, some were quite large. The one reported by Brunswick,⁸ which was 13 by 10 cm, and in its greatest diameter, 15 cm, weighed 673 gm. In the case reported by O'Leary and Womack⁹ the growth was likewise quite large, measuring 11 by 9 by 9 cm and weighing 500 gm. The tumor in Brunswick's case was of especial interest, since because of a previous exploration it was known to have increased in size from about 7 to 15 cm in diameter over a period of four months, nevertheless, and despite the fact that the tumor appeared malignant histologically, there was no gross evidence of metastasis at the time of the second operation.

Surgical Treatment

Once the diagnosis of a probable islet-cell tumor has been made, exploration should be urged, not only for symptomatic relief but also because of the possible danger of damage to the central nervous system produced by repeated attacks of prolonged hypoglycemia and because of the possibility of malignant degeneration of a tumor originally benign.

d with well marked hypoglycemia (blood-sugar concentrations usually below 50 mg per 100 cc) brought on by fasting, increased by physical exertion and relieved by food. The glucose-tolerance test is of aid in diagnosis only if carried out for a sufficient length of time—that is for four to six hours—to allow the blood sugar to fall to an abnormally low level.

Because of the danger of damage to the central nervous system by repeated attacks of prolonged hypoglycemia and because of the possibility of malignant degeneration of a tumor initially benign, early exploratory operation is urged in patients in whom the diagnosis of islet-cell tumor with hyperinsulinism has been made.

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UNRECOGNIZED VESICAL-NECK OBSTRUCTION IN WOMEN*

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MOST urologists are aware of the fact that vesical-neck obstruction in women exists, but not all, I believe, are aware of the fact that it is not an infrequent entity. Although no statistics are available regarding its incidence the condition undoubtedly occurs oftener than is ordinarily appreciated, and I have seen 4 advanced cases in the last two years. Caulk¹ (1921), Nesbit² (1933), Fite³ (1934), Thompson⁴ (1935) and van Houtum⁵ (1935) reported 1 or more cases, and Mirabile⁶ presented a case in 1942. The principal reason for the presentation of the following cases is not only to call attention to this condition again but also to urge that it be recognized early and that its treatment be instituted early enough to avoid the late sequelae of such obstruction. The word "unrecognized" is used to indicate that this condition may easily be overlooked during the routine urologic examination of the patient.

The following brief summaries illustrate the important findings in 3 cases of vesical-neck obstruction in women.

CASE 1 (H. H. 471-447) L. S., a 71-year-old married woman, had had severe urgency, dysuria, frequency and nocturia as often as 10 to 15 times of several months' duration. Prior to this, and for as long as she could remember, she had had difficulty starting urination and had had to get up several times nightly. A stone had been removed from the lower right ureter 4 months previously, with no improvement in the symptoms.

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Urinalysis revealed moderate pyuria and on urinary culture *Aerobacter aerogenes* was grown. On several determinations the residual urine ranged from 600 to 700 cc. Cystoscopy disclosed a large, moderately trabeculated bladder, with an irregular type contracture of the vesical neck and two diverticulae.



FIGURE 1 Case 1. Cystogram showing a large atonic bladder, with two diverticulae.

in the right base of the bladder. A cystogram showed a large, atonic appearing bladder, with two diverticulae (Fig. 1). A urogram revealed mild pyelectasis and a hydronephrosis on the right. The left kidney and ureter appeared normal.

A partial sphincterectomy was performed. 2 gm. of tissue from the posterior vesical lip being removed. Pathologically the tissue consisted of smooth muscle and transitional epithelium.

In reviewing the literature before 1944, Frantz,¹⁰ working with Whipple, found a total of 149 cases of islet-cell tumor with hypoglycemia, including those removed at operation and those found at autopsy, 106 cases were shown to be benign, 28 were questionably malignant and 15 were proved malignant since there were metastases in adjacent organs

Microscopic examination of tumor tissue from the 5 patients with adenoma showed the capsule of the tumor to be incomplete in each of the 4 cases in which enough tissue was available for satisfactory examination (Table 1) In 1 of the 5 cases, questionable blood-vessel invasion was noted This is in keeping with the experience of Frantz,¹¹ who stressed the fact that great difficulty is often encountered in the histologic differentiation of malignant and benign islet-cell tumors Usually, the tumors show encapsulation of varying degrees of completeness, but in some cases there is no capsule and tumor cells are found in the blood vessels Certain patients from whom tumors of questionable type were removed, however, have remained alive many months after operation¹² Frantz¹⁰ states that in the group of questionable tumors the suspicion of the pathologist, not that of the surgeon, has yet to be confirmed in a single case by follow-up data The suggestion is made that these tumors are analogous to the so-called "adenoma malignum" type of carcinoma of the thyroid gland, which is slow growing and late to metastasize At any rate, there is sufficient basis for urging surgical exploration in any patient in whom the diagnosis of probable islet-cell tumor has been made

Experience has shown that if, despite careful search, no tumor is found at operation, the possibility is nevertheless great that a small tumor has been overlooked In most reported cases in which a portion of the pancreas has been resected and no evidence of tumor or adenomatosis found, little or no clinical improvement followed the operation¹⁰ It is well, therefore, to be cautious in making the diagnosis of functional hyperinsulinism—that is, hypoglycemia of chronic, recurrent nature due to hyperfunctioning of islet cells without the presence of a tumor The term "hyperinsulinism" should be reserved for that condition in which excessive secretion of insulin occurs because of overactivity of islet tissue

The approach to the pancreas through a long, curving transverse incision just above the umbilicus and through both rectus muscles has proved satisfactory In the exploration one cannot overemphasize the value of freeing the pancreas thoroughly so that it may be palpated throughout its extent from the tip of the tail to the head, and so that it may be visualized over as large a part of its course as possible This means that infinite pains and patience are required and that at times the operation will be long Of our 6 patients, 2 had

been operated on previously by competent surgeons and yet the tumor was overlooked Palpation must be sufficiently thorough and delicate to disclose a tiny nodule embedded within the substance of the pancreas and not visible from either surface If one is convinced of the diagnosis prior to operation, the exploration should be carried to the limit in an attempt to demonstrate a tumor Even though one nodule has been found, the exploration should be continued because of the relatively high incidence of multiple tumors¹⁰⁻¹² In Maxeiner's¹³ case clinical recovery from attacks of hypoglycemic seizures followed the removal of 75 per cent of the pancreas, examination of the resected portion showed eight small islet-cell tumors If no tumor is found after careful exploration, decision must be made regarding resection of a portion of the pancreas The consensus appears to be that resection under these circumstances should be of radical nature^{14, 15}

It is surprising how well patients withstand manipulation of the pancreas and removal of the tumors With the exception of the patient who had a carcinoma with metastases, all our patients did well postoperatively It is true that one patient developed bronchopneumonia, but the illness was not prolonged and he left the hospital in good condition a month after operation

SUMMARY

Six cases of islet-cell tumor of the pancreas with hyperinsulinism, verified at operation, are reported In 5 cases, removal of a single adenoma resulted in the relief of symptoms that has persisted more than four to seven years after operation In 1 case death followed seven weeks after operation, which disclosed an islet-cell carcinoma, with multiple metastases in the liver

Of the 5 patients with benign adenoma 3 were women and 2 men The ages at the time of operation ranged from sixteen to forty-nine years The period from the onset of symptoms varied from two to eight years In 4 cases the tumor was in the head and in 1 in the body of the pancreas Two of these patients had been operated on previously without the discovery of a tumor

The patient with carcinoma was a woman of fifty-nine years at the time of operation, with symptoms of four years' duration In this case the primary tumor was in the tail of the pancreas

Microscopic examination of tumor tissue from the 5 patients with adenoma showed the capsule of the tumor to be incomplete in each of 4 cases in which there was enough tissue available for satisfactory examination In 1 case questionable blood-vessel invasion was noted

In the 4 cases in which assays were carried out, the insulin content ranged from 3 to over 100 units per gram of tumor tissue

The important features in the diagnosis of islet-cell tumor are the characteristic symptoms associ-

is disconcerting to note that the amount of fibrous tissue found at autopsy in the vesical neck of a series of normal women was similar to that observed in a series of cases of vesical-neck obstruction subjected to transurethral surgery. Furthermore, it seems reasonable to assume that if chronic infection and its accompanying cicatrization were factors the obstruction would be seen much oftener than it is. According to Thompson⁴ it seems almost certain that something other than fibrosis is responsible for the retention of urine in these cases. The theory of imbalance between the sympathetic and parasympathetic innervations of the bladder has also been questioned of late as a result of recent experimental work that has tended to minimize the importance of the sympathetic innervation. In experimental studies the sympathetic innervation was completely excised, with little, if any, alteration in the animal's ability to void. In keeping with this change in the concept of the physiology of micturition the theory of imbalance has received less support.

The presence and the significance of the urethral glands—the so-called “female prostate”—in the development of chronic vesical-neck obstruction has been the subject of much discussion. There is no question that such glands do exist and, when enlarged, actually cause mechanical obstruction or, as is more frequently observed, influence the chronicity of the urethritis and contribute to the resulting cicatrization of the urethra and vesical neck. Although the glands are undoubtedly involved in some cases it is my impression that their role is minor. Questionable glands were present in only 1 of my 4 cases.

The symptoms of chronic vesical-neck obstruction in women are similar to those in men. Urination may be difficult to initiate, or urgency to the point of incontinence may be present. Dysuria, which is usually observed, may be associated with vesical tenesmus and strangury. Frequency and nocturia are usually marked and generally constitute the chief complaints. Recurring hematuria was present in 2 of the cases presented above. The symptoms are usually of long duration, 2 of the 3 patients complained that voiding had been abnormal all their lives. Chronic cystitis is the diagnosis usually made in these cases.

In addition to the general physical examination a careful neurologic and vaginal examination should be performed to exclude the presence of neurogenic vesical dysfunction and to rule out such complicating factors as cystocele, urethral diverticulum and urethral tumor.

The urologic examination should include a routine urinalysis, determination of the residual urine and a careful cystoscopic examination. A cystogram is helpful. Examination of the upper urinary tracts is sometimes quite revealing. Cystometry, although

interesting, was not particularly illuminating or helpful in my cases.

Urinalysis reveals a pyuria of greater or lesser extent, and urine culture yields the usual microorganisms found in lower urinary-tract infections. Microhematuria may also be present.

Determination of the residual urine is perhaps the most significant single test that is made. This is particularly true in cases in which the cystoscopic findings are minimal or inconclusive. If residual urine is present resection of the vesical neck is indicated.

The cystoscopic findings in the advanced cases are usually obvious. Marked trabeculation, cellulose formation, sacculation and diverticula may be present, and all suggest the presence of vesical-neck obstruction as they do in men. The vesical neck itself appears to be contracted and is usually pale, suggesting the presence of cicatrization; it is also rigid and relatively fixed in position. Median-bar formation may be prominent or, as is most frequently observed, an iris-diaphragm type of contracture is present in which the internal vesical orifice actually diminishes in size as the bladder is distended. Cystoscopic visualization of the vesical neck is best performed with a direct-vision cystoscope or, if this is not available, with a for-oblique lens system. The use of a retrograde lens is helpful in that the obstruction may occasionally be more readily recognized from the vesical rather than a urethral aspect.

Early vesical-neck obstruction is difficult to recognize and usually escapes detection. The cystoscopic findings are minimal and at most may consist only of early trabeculation. The vesical neck may or may not appear to be contracted, and there is no residual urine. The most significant finding in my experience is the presence of rigidity in the vesical neck that is discernible when the bladder is completely empty and flaccid. A suspicion of early vesical-neck obstruction is probably the best assistance in its diagnosis.

The ideal treatment in cases of contracted vesical neck consists in removing all the obstructing tissue or in resecting the entire vesical neck or so-called “internal vesical sphincter.” Although this procedure is ideal it is not always necessary, and resection of the posterior vesical lip or median bar is frequently all that is required. Sphincterotomy or incision of the posterior vesical lip, although helpful, is usually of only temporary benefit. Urethral dilatation is the least desirable form of treatment. Following the resection an indwelling catheter is left in for forty-eight to seventy-two hours, after which frequent catheterization and vesical lavage may be necessary to facilitate the return of vesical tone and the elimination of residual urine. Eradication of the urinary-tract infection may be helped with chemotherapy.

The residual urine gradually diminished, and within 2 weeks all symptoms had subsided.

CASE 2 (H H 484-675) B W, a 74-year-old spinster, had been troubled with urgency, dysuria, recurring hematuria, frequency and nocturia of 4 to 10 times as long as she could remember. Urologic examination 3 years previously had revealed "chronic alkaline-encrusted cystitis," and vesical lavage had been advised. Cystoscopy at that time had revealed trabeculation and cellules.

Urinalysis showed grossly turbid, hemorrhagic urine containing *Proteus ammoniae*. The residual urine varied between 90 and 100 cc. Cystoscopy disclosed a markedly trabeculated

A single section of tissue was resected at the midpoint of the posterior vesical neck, followed by dilatation of the urethra. On pathological examination the fragment of the vesical neck consisted of thickened and edematous mucosa.



FIGURE 2 Case 2 Cystogram showing a pyramidal trabeculated bladder, with many cellules

bladder, with many cellules and diffused cystitis. The bladder neck was rigid and contracted. A cystogram demonstrated a pyramidal, trabeculated bladder, with many cellules (Fig 2). Normal upper urinary tracts were seen on a urogram.

A total internal sphincterectomy was performed, 5 gm of tissue being removed from the entire circumference of the vesical neck. Pathological examination revealed tissue composed of smooth muscle and fibrous tissue, with a border lined with stratified squamous epithelium.

Within 6 weeks the residual urine had diminished, and the symptoms were markedly ameliorated.

CASE 3 (H H 528-588) A H, a 73-year-old married woman, complained of hematuria of 3 weeks' duration. Six years previously she had had hematuria, and complete urologic investigation had revealed only cicatricial urethritis. She had also suffered for several years with severe dysuria, mild stress incontinence, frequency and nocturia of 6 times.

On urinalysis moderate pyuria and gross hematuria were demonstrated. On culture *A. aerogenes* was grown. There was approximately 100 cc of residual urine. At cystoscopy the bladder was badly deformed, with multiple cellules and marked trabeculation and dilated ureteral orifices. The vesical neck was rigid and contracted. A moderate cystocele was present. A cystogram revealed a pyramidal bladder with marked trabeculation and multiple cellules in the apex of the pyramid (Fig 3). The base of the bladder was smooth, suggesting the presence of a cystocele. Bilateral ureteral reflux demonstrated a bilateral hydroureter. A urogram showed bilateral hydronephrosis.



FIGURE 3 Case 3 Cystogram showing a pyramidal bladder, with marked trabeculation and multiple cellules in the apex of the pyramid, as well as a cystocele and bilateral ureteral reflux and hydroureters.

with chronic inflammatory changes in the submucosa. Several small foci of epithelium present below the surface were slightly cystic and suggested cystitis cystica.

The hematuria subsided and the patient's symptoms improved greatly. Nocturia of 2 times persisted. The residual urine diminished to 10 cc.

The advanced ages of these patients and of another patient not reported indicate that in women this condition is usually present in the older age groups, as it is in men. Of the cases reported in the literature the greatest number were in this same age group. "Prostatism sans prostate" seems a particularly appropriate term to describe this group of cases.

The etiology of vesical-neck obstruction in the female is not definitely established. Perhaps the most popular theory is that the obstruction is due to a contracture of the vesical neck resulting from sclerosis or fibrosis at this site, the fibrosis being attributed to chronic low-grade inflammation of the urethra or to vaginal trauma. Some observers believe that the contracture is due to hypertrophy of the muscle fibers at the vesical neck and is not the result of cicatrization at this site. Another point of view is that the obstruction is fundamentally physiologic and due to dysectasia or achalasia—in other words, to a failure of the vesical neck to relax as the bladder contracts. This theory implies that the innervation of the bladder and vesical neck is at fault, and an imbalance between the sympathetic and the parasympathetic innervations is considered responsible.

In the light of present knowledge no one explanation is completely satisfactory. Although the theory of fibrosis of the vesical neck seems plausible enough,

ever pain and collapsed. She died on the operating table. An aneurysm of the left renal artery was discovered. Eiss,⁵ who reported 2 fatal cases of retroperitoneal hemorrhage in men, stated that the differential diagnosis in women must include the following: ectopic pregnancy, perforated gastric ulcer, appendicitis, and if trauma is a factor, a ruptured viscus. He believed that there must be prompt exploration to find the cause. When the hemorrhage is retroperitoneal the abdomen should be closed immediately and the shock treated. He stated that a careful search of the literature revealed only 7 cases similar to the 2 he reported. Lāwen⁶ also reported 2 fatal cases in men. One patient had a preoperative diagnosis of left perirenal hemorrhage, and a retroperitoneal operation was performed. Autopsy revealed a large left retroperitoneal hemorrhage from a perforation of the inferior vena cava at its junction with the left common iliac vein. There was a chronic inflammatory infiltration of the wall of the vein (phlebitis dissecans) and also an old thrombophlebitis, which he believed secondary to a chronic knee condition. The other patient had right renal colic, and the preoperative diagnosis was retroperitoneal tumor. Extraperitoneal operation revealed a cyst containing 1000 cc of old blood. The cyst wall was formed probably by organization of the peripheral parts of the hematoma. The kidney, as part of the wall, was removed. Seven weeks after operation the patient collapsed. A large cavity filled with blood, which was found after entry through the old incision, was emptied and packed. The patient finally died of pulmonary embolism. Post-mortem examination revealed sarcoma of the lumbodorsal fascia, with metastases scattered in various areas.

Halban⁷ believed that a retroperitoneal hemorrhage is nearly always perirenal at the start, that it may be secondary to tuberculosis or tumor of the kidney and that it may also occur spontaneously in nephritis and hemophilia. He stated that the bleeding caused by trauma, tuberculosis and tumor is of no special interest but that the spontaneous, essential hemorrhages, in spite of many observations, have not yet been fully explained.

The following case report is unique in two respects: it is the only case of retroperitoneal hemorrhage complicating pregnancy with recovery that has been reported, and describes for the first time a new entity causing dystocia.

CASE REPORT

B. F., a 38-year-old woman, had been married for 12 years. A child, weighing 6 pounds, 12 ounces, had been born 11 years previously; the pregnancy, delivery and convalescence had been normal. The past history revealed an appendectomy at the age of 26 but no serious medical illnesses. The menstrual history was normal. The patient's father and mother and three siblings were living and well, there was no history of the usual familial diseases. The last menstrual period had begun on February 2, 1945, and confinement was expected on November 24.

Physical examination was negative. On the first visit on June 5 the uterus, which was enlarged about two thirds the

way to the umbilicus, seemed slightly firmer than usual. The impression was gained that the uterus was slightly larger than the dates indicated, but the patient was not absolutely sure of the date of the last catamenia. The weight was 140 pounds. The blood pressure was 150/90, and the pulse 80. Examination of the blood revealed a red-cell count of 4,010,000, with a hemoglobin of 72 per cent (Sahl). The blood was of Group 0 and was Rh—. The blood Hinton reaction was negative.

The patient had an uneventful pregnancy. Vaginal examination on November 17, approximately a week before the expected date of confinement, revealed a cervix that was partly taken up and soft and slightly anterior to the usual position. It admitted a finger readily. The presenting part, however, was not definite. On December 1 the patient was admitted to the Cambridge Hospital because of moderate pain in the left side. Physical examination revealed slight tenderness along the course of the ureter, there was no costovertebral tenderness. The uterus was soft, and the fetus appeared to be slightly less than average size. The temperature was 99.2° F., and the pulse 92. A catheterized specimen of the urine was taken, the report of the sediment was equivocal—there were said to be 40 or 50 white cells per high-power field. An anteroposterior film revealed a fetus of a size consistent with an 8 months' pregnancy and in a left occipitoanterior position, the head was unusually high. Vaginal examination revealed a tender, moderately firm mass filling the posterior part of the pelvis and pushing the cervix up behind the symphysis. The diagnosis was probable fibroid of the lower segment of the uterus causing dystocia. Cesarean section was deemed advisable.

At operation on December 5 under continuous spinal anesthesia employing 6 mg. of pontocaine, the usual midline incision was made below the umbilicus and the abdomen was opened. A small amount of blood was found in the left side of the lower abdominal cavity. The bladder flap, which was somewhat soggy and thin, was stripped from the uterus, and a transverse incision was made in the lower segment. A female infant weighing 5 pounds, 6 ounces, was extracted. The uterus was brought out of the incision for examination of the abdomen. Whereas previous to the incision in the uterus, the examiner's hand had been passed around the uterus without palpating a fibroid, inspection revealed a large, firm, retroperitoneal hemorrhage that filled the whole true pelvis and extended well into the mesentery of the sigmoid, which was ribboned out over the hemorrhagic mass. The diagnosis was retroperitoneal hemorrhage in the true pelvis causing dystocia. It was decided that the best treatment was to leave the hemorrhagic area undisturbed. The placenta had been delivered while the character and extent of the mass were being investigated. The uterus was closed with No. 1 catgut in two layers. Five grams of sulfanilamide was placed under the bladder flap, which was overlapped with a fine suture. The abdomen was closed in layers, No. 1 chromic catgut being used for the peritoneum and fascia and silk for the skin.

There was no excessive bleeding from the incision or the uterus, and the postoperative condition was good. On December 6 the temperature was 100.6° F., and the pulse 106 to 150. Distention was slight. Rectal examination revealed that the mass could be readily felt and was still tender. Two days later the temperature varied from normal to 99.2° F. There was no distention. The general condition was good. On December 14, when the patient was allowed to sit up, the temperature still varied from normal to 99.2° F. Otherwise, the general condition was excellent. The patient was discharged on the 15th day.

Pelvic examination on February 23, 1946, revealed a slightly tender, firm mass—about 5 cm. in diameter—posterior to the cervix but not projecting far into the vagina. The hematoma was evidently being absorbed slowly. There was slight to moderate discomfort in the left lower abdomen. On May 20, when the patient still complained of vague back and lower abdominal discomfort, examination revealed slight tenderness behind the cervix, but the hematoma, which was smaller, was palpated with difficulty.

SUMMARY

Retroperitoneal hemorrhage complicating pregnancy is extremely rare but probably occurs more frequently than reports indicate. One type is characterized by severe abdominal pain and shock as a

SUMMARY

Three cases of chronic vesical-neck obstruction in women are presented in which resection of all or part of the vesical neck was performed with satisfactory relief of symptoms.

Attention is drawn to the facts that the condition is not infrequent and that dire consequences, in the form of dilatation of the upper urinary system, may ensue if treatment is not instituted early in the course of the disease.

A search for the presence of early vesical-neck obstruction in every case of chronic cystitis in women

is urged, so that this condition may be recognized and adequate treatment instituted.

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RETROPERITONEAL HEMORRHAGE] COMPLICATING PREGNANCY*

Report of a Case

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IN 1918 Potocki¹ reported a case of retroperitoneal hemorrhage complicating pregnancy in which the patient, two and a half months' pregnant, experienced pain in the lower abdomen after intercourse. The pain extended gradually to the left side, with some degree of shock. Shortly after admission to the hospital the pain became severer and the shock deeper. The diagnosis was ruptured tubal pregnancy or pregnancy with an ovarian cyst with a twisted pedicle. Laparotomy performed immediately revealed an extensive retroperitoneal hemorrhage that did not involve the true pelvis but filled the mesocolon and the retroperitoneal areas in the region of the pancreas, left kidney and stomach. The patient died on the operating table. Autopsy did not disclose the bleeding vessel. It was concluded that a major vessel had perforated because 1200 to 1800 cc of blood was present retroperitoneally. The left kidney was found to be tuberculous, and a large hematoma surrounded the kidney. Potocki believed that the probable cause of the hemorrhage was a miliary aneurysm of the renal artery. His search of the literature failed to reveal any other case occurring in pregnancy, but disclosed similar cases in men, one of which was a spontaneous fatal hemorrhage from a psoas-muscle vessel. In another case severe pain developed in the left side of the abdomen, and a mass could be felt in the left renal region, the patient died on the operating table, and post-mortem examination revealed a large retroperitoneal hemorrhage, small abscesses in the kidney and stones. A third patient, who had syphilis, died of a cerebral accident, and autopsy disclosed a large retroperitoneal hemor-

rhage that was believed to have started from the renal artery, since there was a history of an old perirenal abscess. Potocki concluded that pregnancy did not predispose a patient to this condition and believed that in most cases the hemorrhage started from renal vessels.

Low,² in 1944, reported a fatal case in pregnancy. The patient, within two weeks of term, was admitted to a hospital several hours after being seized with violent pain originating in the left upper quadrant of the abdomen and extending to the back. The pain occurred after a bowel movement, and shock ensued shortly after its onset. A transfusion was given, and a classic cesarean section was performed. A moderate amount of blood-stained fluid was found in the abdomen, but the essential finding was a massive retroperitoneal hemorrhage extending from above the left brim of the true pelvis and behind the sigmoid, descending colon and splenic flexure, across the midline of the upper abdomen and apparently most marked in the region of the spleen and left kidney. The patient died seven hours after operation, in spite of another transfusion. Post-mortem examination revealed all the large arteries to be relatively thin walled, and the left ovarian artery to be particularly so, as well as dilated and tortuous and presenting some aneurysmal dilatation near its origin. Kenny,³ in 1945, reported a similar case in which the patient, who had pre-eclampsia and was at term, had pain and shock following intercourse. A retroperitoneal hemorrhage extending from the pelvic brim to the diaphragm was discovered. The source of the bleeding was not found at autopsy. Kenny believed that the source of the hemorrhage was the retroperitoneal capillaries.

Wilson⁴ delivered normally at full term a patient who twenty-six hours post partum experienced

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the divergent results were due in some degree to the unreliability of the chemical methods available. Technical difficulties arising from the small amounts of material used, impurities in the framework of the tablets and errors arising from colorimetric analysis are a few of the factors that contributed to the unreliability of these reports.

The fall in blood pressure in anesthetized rabbits after intravenous administration of small amounts of nitroglycerin was utilized as a method of biologic assay for nitroglycerin deterioration by Edmunds and Roth¹⁵. On the basis of their findings they concluded that tablets not more than two years old had lost practically none of their strength but that older tablets had deteriorated to some extent.

Although the results of chemical and biologic assay methods when applied to the question of deterioration of nitroglycerin with age have not been conclusive, it is generally believed by pharmaceutical manufacturers and clinicians that nitroglycerin is not a stable preparation. Accordingly, current medical opinion, as expressed in leading textbooks of cardiology and general therapeutics, recommends that patients employing nitroglycerin for the treatment of angina pectoris discard old tablets and purchase fresh ones every three to six months.

MATERIAL AND METHODS

The clinical potency of readily soluble hypodermic tablets of nitroglycerin of varying age in doses of 0.6, 0.4, 0.3, and 0.1 mg (1/100, 1/150, 1/200 and 1/500 gr) were investigated. Fifteen different preparations were tested. Three were fresh tablets (less than two months old). Three others had been on the laboratory shelves in pasteboard pillboxes for periods ranging from three to five years. Five were obtained from the shelves of retail drugstores and pharmaceutical houses, where they had remained for four to eleven years, no special precautions against deterioration had been taken in packaging and storage. Three samples originally less than two months in age were kept in pasteboard pillboxes in an incubator at 37° C for three additional months to ascertain the effect of heat on their clinical effectiveness. The remaining sample consisted of fresh readily soluble hypodermic tablets (0.3 mg) that had been kept in a loosely fitting screw-cap vial and carried by 2 patients for four months close to the body in the same vest or trousers pocket used for carrying their clinical supply of nitroglycerin.

Five male patients with angina pectoris, who had demonstrated a moderate to marked response following sublingual administration of nitroglycerin, were selected for these studies. The patients had been followed in a special clinic at weekly intervals for periods ranging from six months to eleven years. The amount of exercise each patient could perform before developing an attack of angina pectoris, as demonstrated by the standardized exercise tolerance test, had been determined on many occasions ac-

cording to a method previously described¹⁶. The exercise, which consisted in mounting and descending a two-step staircase in a room maintained at a temperature of 45 to 50° F, was carried out approximately an hour after the patient had had a light breakfast and had rested for half an hour in the clinic. Only one test was attempted on any given day. The number of trips each patient could perform gave a measure of the exercise tolerance. During the period of study the patients were given only placebo medication except for nitroglycerin as needed in their everyday activities.

The exercise tolerance as determined on many occasions without medication was used as the control for the subject concerned. As a further check the exercise tolerance was measured two minutes after the sublingual administration of blank hypodermic tablets indistinguishable in appearance from the nitroglycerin used in the study. The results were compared with those ascertained two minutes after sublingual administration of fresh and old (three to eleven years old) tablets of nitroglycerin.

The amount of exercise necessary to induce angina, under the standardized conditions of the test when either no medication or blank hypodermic tablets were administered, varied in all but 1 case between 5 and 17 per cent of the average exercise tolerance for the patient. The clinical effectiveness of nitroglycerin was indicated by an increase in exercise tolerance of 25 to 100 or more per cent over the maximum amount of work possible under the control conditions.

RESULTS

The sublingual administration of fresh hypodermic tablets of nitroglycerin prior to exercise increased the exercise tolerance of each patient by 25 to 100 per cent or more (Table 1). The increment of exercise induced by each preparation of nitroglycerin was essentially the same, despite a dosage range of 0.6 to 0.1 mg, except in a patient (L. S.) who showed a moderate response only to a dose of 0.6 mg. In 2 cases, after the administration of nitroglycerin, the patients were able to exercise to the point of fatigue or development of leg pain without precipitating angina pectoris.

Sublingual administration of blank hypodermic tablets did not result in an increase of ability to work.

The exercise tolerance following the administration of eight different samples of nitroglycerin three to eleven years old was the same as that following fresh nitroglycerin, regardless of the age of the tablets and the lack of special precaution in packaging and storage. The rate at which the tablets dissolved under the tongue was also unaffected by age, since all patients reported that each tablet dissolved in from ten to thirty seconds after the sublingual administration. Similarly, the speed of response was unaffected by age, for all tests were conducted two

result of massive retroperitoneal hemorrhage in the upper abdomen. The most frequent source of the hemorrhage is disease in the kidney and its vessels. The condition is usually fatal. The other type, reported above for the first time, is a retroperitoneal hemorrhage occurring chiefly in the true pelvis and resulting in a tumor causing dystocia and necessitating cesarean section.

The source of the hemorrhage in the case reported was probably one of the hemorrhoidal veins. Such a hemorrhage should not be evacuated, its complete absorption may take months.

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THE EFFECT OF AGE ON THE CLINICAL EFFECTIVENESS OF NITROGLYCERIN TABLETS*

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BOSTON

THE value of sublingual administration of nitroglycerin for relief of attacks of angina pectoris is well established. Nitroglycerin has also been advocated as a prophylactic—before exercise and so forth—to prevent pain.¹⁻³ Objective measurements of the value of both these therapeutic uses have been reported.^{2, 4, 5}

From a practical point of view, the stability of nitroglycerin tablets is important. In the past, many lots of nitroglycerin have been condemned as substandard, presumably because of deterioration. As a result, fresh tablets are recommended, to be dispensed in tightly stoppered bottles.

The question of deterioration of nitroglycerin is still controversial. No definite standards of freshness have been established, and no simple methods of analysis are available. None of the numerous procedures of chemical or biologic assay used for testing the deterioration of nitroglycerin yield information concerning the most significant clinical aspect—namely, the efficacy in the treatment of angina pectoris. This aspect can be measured readily by determining the exercise tolerance, under carefully standardized conditions, of patients with and without the use of nitroglycerin at varying periods after manufacture.

The purpose of this communication is to report the effect of age and heat on the clinical effectiveness of hypodermic tablets of nitroglycerin as determined in patients with angina pectoris. Only hypodermic tablets were tested because attacks of angina pec-

toris are short in duration, and hence rapidly dissolving hypodermic tablets are preferable to triturated ones.^{2, 3}

The various chemical methods that have been proposed for quantitative analysis of the small amounts of nitroglycerin present in medicinal preparations have been summarized by Hutchinson.⁶ In general, they consist of extraction of the nitroglycerin, its reduction into one or more of its breakdown products (nitrogen, nitrate salts, nitrite salts or ammonia), determination by colorimetric or gaseous analysis of the amount of this product and computation therefrom of the amount of nitroglycerin present in the original preparation. The official assay method of *U S P XII*, for example, consists of repeated ether extraction of no less than twenty finely powdered nitroglycerin tablets, evaporation of the ether and saponification of the nitroglycerin in the presence of potassium permanganate. Devarda's alloy is then added to the mixture, and the nitrate present is thereby reduced to ammonia. This is distilled into a standard solution of sulfuric acid, and the amount of unneutralized sulfuric acid is determined by titration with sodium hydroxide, methyl red being used as an indicator. The amount of nitroglycerin originally present is computed from these figures. Blank determinations with the same quantities of reagents are performed in a similar manner, and the necessary corrections made.

Deterioration of nitroglycerin tablets with age has been investigated by chemical determination of the nitroglycerin content at varying times after manufacture. The results, however, are controversial. Scoville,⁷ Smith⁸ and Meek⁹ found significant loss of nitroglycerin in tablets assayed up to four years after manufacture, whereas Bergenaui,¹⁰ Rippetoe and Smith,¹¹ Vanderkleed,¹² Snyder¹³ and Francis¹⁴ reported no significant loss in tablets assayed at periods up to eight years after manufacture.

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MATERIAL AND METHODS

The clinical potency of readily soluble hypodermic tablets of nitroglycerin of varying age in doses of 0.6, 0.4, 0.3, and 0.1 mg (1/100, 1/150, 1/200 and 1/500 gr) were investigated. Fifteen different preparations were tested. Three were fresh tablets (less than two months old). Three others had been on the laboratory shelves in pasteboard pillboxes for periods ranging from three to five years. Five were obtained from the shelves of retail drugstores and pharmaceutical houses, where they had remained for four to eleven years, no special precautions against deterioration had been taken in packaging and storage. Three samples originally less than two months in age were kept in pasteboard pillboxes in an incubator at 37° C for three additional months to ascertain the effect of heat on their clinical effectiveness. The remaining sample consisted of fresh readily soluble hypodermic tablets (0.3 mg) that had been kept in a loosely fitting screw-cap vial and carried by 2 patients for four months close to the body in the same vest or trousers pocket used for carrying their clinical supply of nitroglycerin.

Five male patients with angina pectoris, who had demonstrated a moderate to marked response following sublingual administration of nitroglycerin, were selected for these studies. The patients had been followed in a special clinic at weekly intervals for periods ranging from six months to eleven years. The amount of exercise each patient could perform before developing an attack of angina pectoris, as demonstrated by the standardized exercise tolerance test, had been determined on many occasions ac-

cording to a method previously described¹⁶. The exercise, which consisted in mounting and descending a two-step staircase in a room maintained at a temperature of 45 to 50° F, was carried out approximately an hour after the patient had had a light breakfast and had rested for half an hour in the clinic. Only one test was attempted on any given day. The number of trips each patient could perform gave a measure of the exercise tolerance. During the period of study the patients were given only placebo medication except for nitroglycerin as needed in their everyday activities.

The exercise tolerance as determined on many occasions without medication was used as the control for the subject concerned. As a further check the exercise tolerance was measured two minutes after the sublingual administration of blank hypodermic tablets indistinguishable in appearance from the nitroglycerin used in the study. The results were compared with those ascertained two minutes after sublingual administration of fresh and old (three to eleven years old) tablets of nitroglycerin.

The amount of exercise necessary to induce angina, under the standardized conditions of the test when either no medication or blank hypodermic tablets were administered, varied in all but 1 case between 5 and 17 per cent of the average exercise tolerance for the patient. The clinical effectiveness of nitroglycerin was indicated by an increase in exercise tolerance of 25 to 100 or more per cent over the maximum amount of work possible under the control conditions.

RESULTS

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Sublingual administration of blank hypodermic tablets did not result in an increase of ability to work.

The exercise tolerance following the administration of eight different samples of nitroglycerin three to eleven years old was the same as that following fresh nitroglycerin, regardless of the age of the tablets and the lack of special precaution in packaging and storage. The rate at which the tablets dissolved under the tongue was also unaffected by age, since all patients reported that each tablet dissolved in from ten to thirty seconds after the sublingual administration. Similarly, the speed of response was unaffected by age, for all tests were conducted two

minutes after sublingual administration of the tablets

The tablets that had been stored in pasteboard pillboxes in the incubator at 37° C for three months showed complete loss of clinical potency. The amount of exercise each patient could perform after

ness of the preparations tested regardless of their actual nitroglycerin content. This method, which has been used in this clinic for over ten years, has been found to offer a satisfactory objective measure of the effect of various medications in patients with angina pectoris.^{17, 18} By employing the patient him-

TABLE 1 *Effect of Nitroglycerin on Patients with Angina Pectoris as Measured by Exercise Tolerance Test (in Trips)*

PATIENT	No Medi- cation	Blank Tab- lets	Fresh Nitrolycerin Tablets			Old Nitrolycerin Tablets*										Incubated Nitro- lycerin Tablets			Nitro- lycerin Tablets Carried in Pocket
			0.6 mg	0.3 mg	0.1 mg	3-5 yr. old	4 yr old	5 yr old	9 yr old	10 yr old	11 yr old	0.6 mg	0.3 mg	0.1 mg	0.6 mg	0.3 mg	0.1 mg		
E B	16-22	18-24	28†	29†	37†	29†	28†	37†	30†	30†	27†	34†	26†	24	22	21	23†		
S R	26-30	28	56	55	47	59	47-61	51	54	56	50	46	60	32	30	30	56		
S W	24-30	24	45†	50†	49†	50†	52†	47†	42†	52†	46†	45†	48†	31	30	30	35†		
B H	17-18	20	42	63	49	63	60	49	55	60†	70†	42	53†	25	19	18	60†		
L S	18-20	17	25	20	21	27	16	22	17	30	27	20	17	14	19	18	34		

*Tablets stored in following types of containers: pasteboard pillboxes, brown screw-cap bottles, clear screw-cap jars, and clear tablet vials with cork stoppers.
†Exercise stopped because of fatigue or intermittent claudication, not angina pectoris.

sublingual administration of these tablets in dosages of 0.6, 0.3 and 0.1 mg was essentially the same as that performed without medication or following administration of blank hypodermic tablets.

The tablets that had been carried close to the body for four months showed no loss of clinical potency.

DISCUSSION

Direct transference of the results of chemical or biologic assay methods to the problem of clinical potency of old nitroglycerin preparations is not justifiable. It has been shown that for all practical purposes 0.3 mg is as effective as larger doses and, furthermore, that tablets containing as little as 0.1 mg of nitroglycerin are of clinical value.^{2, 3} A decrease in the nitroglycerin content of old tablets, therefore, may not indicate a corresponding reduction of clinical value in patients with angina pectoris.

The clinical response following sublingual administration of nitroglycerin in 4 patients was essentially the same in dosages ranging from 0.6 to 0.1 mg. On that basis it might be postulated that old tablets of 0.6 mg could lose up to 80 per cent of their nitroglycerin and still retain clinical potency and value. To determine if this were so, the nitroglycerin content of several 0.6-mg tablets employed in this investigation was determined by the *U S P* method of chemical assay (Table 2). Comparison of the content of the three old samples with that of the fresh tablets showed no significant loss of nitroglycerin. Furthermore the results in a patient (L S) who responded to 0.6 mg but not to a dose of 0.4 mg or smaller indicate that 0.6-mg tablets as old as nine years failed to deteriorate appreciably in clinical value.

The method of biologic assay employed in this investigation gave a measure of the clinical effective-

ness of the preparations tested regardless of their actual nitroglycerin content. This method, which has been used in this clinic for over ten years, has been found to offer a satisfactory objective measure of the effect of various medications in patients with angina pectoris.^{17, 18} By employing the patient him-

self as a means of testing clinical efficiency the procedure avoids the difficulties that are inherent in the chemical or biologic methods of assay previously employed. With the exception of the tablets exposed to heat, all preparations, regardless of age, showed no loss of clinical potency. These results indicate that, under ordinary conditions of storage in a retail drugstore, hypodermic tablets of nitroglycerin retain their clinical effectiveness for many years. Further

TABLE 2 *Chemical Assay of Four Preparations of Nitroglycerin**

AGE OF TABLETS	PERCENTAGE OF ORIGINAL NITROGLYCERIN CONTENT
Fresh	104
Three to five years old	103
Five years old	78†
Nine years old	99

*These analyses were carried out by Dr. Bibbins, of the Pharmaceutical Department of Eli Lilly and Company, without knowledge of the age or the manufacturer of the four specimens.
†These tablets were soft and the edges had worn off.

more, under ordinary conditions of use by patients, they retain their effectiveness for at least four months. Therefore, it is not necessary for patients to purchase fresh supplies at more frequent intervals.

Tablets exposed to heat, however, rapidly lose their clinical effectiveness. This fact should be kept in mind when nitroglycerin preparations are stored. The tablets do not lose their clinical potency if kept at room temperature, but if they are kept near steam pipes, radiators and so forth, they are apt to suffer deterioration.

SUMMARY

The clinical effectiveness in patients with angina pectoris of eleven preparations of hypodermic tablets

nitroglycerin, in dosages ranging from 0.6 to 0.1 g, were assayed at periods varying from a few months to eleven years after manufacture. No particular precautions against deterioration had been observed in the packaging and storage of these tablets. There was no essential loss of clinical effectiveness in the old tablets as compared to fresh tablets of the same dosage.

Fresh tablets exposed to heat (37° C) for three months showed a complete loss of clinical potency, whereas tablets that had been carried by patients in the customary manner for four months showed no loss of clinical effectiveness.

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MEDICAL PROGRESS

THE DIAGNOSIS OF CANCER OF THE PANCREAS*

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BOSTON

TEN years ago Clute¹ discussed the problems presented by the diagnosis and treatment of cancer of the pancreas. In the intervening decade surgical treatment has progressed remarkably,²⁻⁴ but diagnosis is still lagging, partly owing to the variability of pancreatic symptoms, the inaccessibility of the pancreas to examination, the difficulty of x-ray study of this gland and the unavailability of an easy and reliable function test. On the other hand, failure to recognize the symptoms that have been repeatedly emphasized in the literature of the last ten years and to institute such tests as have been made available are also responsible for the late recognition of pancreatic carcinoma.

The intimate anatomic relation of the head of the pancreas to the ampulla of Vater and its adjoining structures (the papilla of Vater, the terminal common bile duct, the duct of Wirsung and the duodenal mucosa covering the papilla) makes the exact site of origin of many cancers in this area uncertain. Although occasionally possible, the clinical differentiation between cancers of the pancreas and those of the ampullary region is particularly difficult. Any clinical consideration must consequently encompass neoplasms arising at both sites. Cancers of the islands of Langerhans, on the contrary, are charac-

terized by a different syndrome and are not included in this discussion.

The literature as reviewed by Leven⁵ in 1933 indicated that cancer of the pancreas afflicts the usual cancer age group between forty and seventy, attacks men two or three times as frequently as women and occurs roughly once in every thousand hospital admissions. Berk's⁶ extensive review in 1941 confirmed these figures. He was also led to conclude that "carcinoma of the pancreas causes 1 to 2 per cent of all deaths in the population at large," a somewhat puzzling statement because Berk at the same time agreed with previous writers that cancers of the pancreas account for 1 to 2 per cent of all cancers. Since the publication of Berk's review, a number of articles have dealt with the incidence of pancreatic carcinoma,⁷⁻¹³ but no trends have been observed that challenge the principal conclusions reached by Leven and Berk. It is to be noted, however, that youth provides no guarantee against pancreatic neoplasm. In 113 cases collected in two series 6 patients were under the age of forty,^{7, 13} and up to 1941, pancreatic or periampullary cancer had been reported nine times in patients less than twenty years old.⁹ Periampullary carcinoma, in particular, may appear in younger persons.¹⁴

Although opinion regarding the general incidence of pancreatic carcinoma is quite consentaneous, statements on the relative incidence of cancers of the

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ampullary area, of the head and of the body and tail of the pancreas are more conflicting. The diverse results reported by various authors probably depend on two factors: the methods used in making the diagnosis, and the type of material included in the study. Diagnoses made on purely clinical grounds are obviously subject to error, but incorrect conclusions may also be drawn after the pancreas is palpated at operation and a biopsy taken.³ Accurate diagnosis is made possible only by autopsy or by operative procedures that resect large blocks of tissue. The experience of Ransom¹⁵ is illustrative of 10 patients examined at laparotomy, 6 were considered to have pancreatic carcinoma and 4 ampullary neoplasms, whereas autopsy revealed that only 3 of these patients had cancer of the pancreas, in 7 cases the primary site was the common bile duct.

Whether the diagnosis is made at operation or post mortem also affects the material included in an analysis of cases. Patients observed at operation contain a preponderance of cancers of the ampulla or of the head, for cases of this type present symptoms calling for operative intervention. Cattell,³ for example, states that carcinoma of the ampulla is more frequent than that of the pancreas. A series based on material at autopsy, however, may reveal that lesions of the tail of the pancreas occur much oftener than one would suspect after analyzing surgical material.¹⁶ Finally, the diffuse nature of many pancreatic cancers makes it merely a matter of individual opinion whether or not the primary lesion is placed in the head.⁶ As a rough approximation, however, one may expect to see three cancers of the head of the pancreas for every one that involves the body and the tail. The relative frequencies of pancreatic and periampullary lesions are indicated by the following figures: cancers of the pancreas have been reported in 0.30 to 0.75 per cent of all autopsies,⁶ whereas the incidence of periampullary carcinomas is said to range from 0.04 to 0.20 per cent.^{17, 18} of all post-mortem examinations.

For many years it has been the practice to separate cancers in the head of the pancreas from those in the tail on the basis of clinical and pathological differences. The wisdom of this practice has been challenged by Berk,⁶ who emphasizes the difficulty of diagnosing and delineating pancreatic neoplasms, and who suggests that overemphasis of the single symptom of jaundice interferes with a broad conception of the symptoms and signs to be expected in all cases of pancreatic cancer. Another frequently quoted difference — that cancers in the ampulla or head grow slowly and metastasize late, whereas those in the body and tail grow and spread rapidly — may be more apparent than real. That this difference has been observed at autopsy or at operation is unquestioned. In 28 patients dying of ampullary carcinoma, Baggenstoss¹⁸ found no evidence of metastases in 15, in the 16 cases of cancer of the body or tail reported by Duff,¹⁶ metastases were present

in all but 1. Perhaps an intrinsic difference between the two lesions exists, but the influence of other factors is excluded with difficulty. Lesions in the head of the pancreas usually obstruct the hepatic or pancreatic ducts, and the resultant chain of events leads either to surgery or to death on the basis of hepatic or pancreatic failure before the neoplasm has a chance to grow or spread. In cancers of the body and tail, however, no vital processes are disrupted by the primary growth, and the patient slowly dies of cachexia and inanition as the cancer invades and metastasizes. This rather obvious explanation of the apparent difference between cancer in the head and tail of the pancreas has, of course, been recognized by various writers but has been dismissed as a contributory factor on the basis of various theoretical arguments.^{18, 19} That the dismissal is somewhat premature, however, is indicated by the observations of Orr,²⁰ who successfully removed periampullary carcinomas in 8 patients, 5 of whom subsequently died of metastases.

Heterotopic pancreatic tissue occurs in various portions of the digestive tract, but the duodenum, stomach and jejunum are the most frequent sites. Like other pancreatic tissue, these aberrant cells are subject to malignant degeneration²¹ and may account for some of the cancers of the small bowel.²²

The factors that make it difficult to collect accurate statistics on the pathology of pancreatic and ampullary cancers also introduce discrepancies into an analysis of the symptoms produced by these diseases. The incidence of jaundice may serve as illustration. Since this finding is the usual reason for surgery in patients with pancreatic neoplasm, its occurrence in surgical material is practically constant. Except in pancreaticoduodenectomy the surgical diagnosis of cancer of the pancreas depends on palpation of a nodule or mass in the head of the gland, metastases or an occasional biopsy attesting to the malignant nature of the process. In a series of surgical cases jaundice is consequently found to be the outstanding symptom of pancreatic carcinoma. A pathologist, however, might classify many of the nodules in the head of the pancreas as periampullary neoplasms. Deprived of these cases and increased by relatively nonicteric cases of pancreatic cancer, a series studied at autopsy reveals that jaundice is a frequent but far from invariable symptom of pancreatic cancer.

The marked effect that the diagnostic method may have on the observed incidence of a symptom and the variability of the methods from one series to another suggests that the true incidence of jaundice — or of any other symptom — cannot be derived merely by the process of averaging the incidences reported by all who have discussed cancer of the pancreas. Such averages are at best approximations, and the assignment of an exact figure carried to two decimal places to the incidence of any symptom of pancreatic cancer seems to impart an

warranted aura of accuracy. Nevertheless, three symptoms occur so frequently that there is no doubt concerning their prevalence. These symptoms are weight loss, pain and jaundice.

Weight loss, sometimes totaling as much as 50 pounds, is almost invariably evident, only a rare case report states that the patient had lost no weight when first seen.^{23, 24} One may question whether this loss, particularly one of 20 pounds or more, does not indicate advanced disease and preclude operability. In some cases weight loss carries such an implication, especially if the neoplasm arises in the body or tail of the pancreas. In others, however, weight loss occurs because a small periampullary neoplasm obstructs the flow of digestive juices. In lesions of this type weight loss certainly does not contraindicate operation, as is evident from Cattell's³ figures. Of 18 patients who were subjected to pancreatic resection, 16 had experienced preoperative weight loss, 13 had ampullary lesions and 13 enjoyed what appeared to be a successful result. When weight loss is the manifestation of a carcinoma in the head of the pancreas, its significance is variable; it may mean that the growth is inoperable, but it may also be the result of an associated diabetes, or of a widespread destruction of the acinar elements or of secondary gastrointestinal disorders such as nausea and diarrhea. A patient whose case was recently reported, for example, had lost 50 pounds because of an extensive pancreatic cancer, yet a total pancreatectomy was feasible, and the patient appeared to be doing well a year after operation.²⁵ One must conclude that progressive weight loss is an important symptom not only of all pancreatic cancers but also of those susceptible to operative removal.

Pain ranks as the second most significant symptom of cancer of the pancreas. The association of painless jaundice with pancreatic carcinoma seems to be so firmly rooted in the medical mind that almost every recent writer on this subject has felt it necessary to emphasize repeatedly that at least three fourths of the patients with cancer of the pancreas do have pain. Ampullary cancers are said to occasion less pain and are held responsible for many cases of painless jaundice,^{3, 9, 26} but in one series more than half the patients studied complained of pain.¹⁰ The character of the pain in pancreatic or ampullary cancer is extremely variable and can be misleading in that it may mimic biliary or intestinal colic. In many cases, however, its features are almost specific: it is dull, boring and often severe. It is located in the upper abdomen, either on the right or on the left, and radiates through to the back.^{27, 28} It is not related to eating, bowel movements or physical activity, but is often aggravated when the patient lies on his back. In such cases the patient usually complains that the pain is worse at night, and the attending physician may find "a nervous, apprehensive patient sitting up in bed,

bending forward over folded arms which rest against his epigastrium, and maintaining his position hour after hour because it gave the most relief from pain."²⁴ Cases of this type should be suspected of being cancer of the pancreas and should not be classified as psychoneurosis or back strain.

Careful pathological examination indicates that neoplastic invasion of nerves occurs in many cases of pancreatic carcinoma.²⁹ In addition to the deep somatic nerves, the celiac plexus of sympathetic nerves is presumably most subject to invasion by reason of its position adjacent to the pancreas. Since both the somatic and sympathetic nerves can transmit pain impulses, it is possible that back pain in pancreatic cancer is produced in part by neural invasion. Actually, a fair but not a perfect correlation between back pain and invasion of the nerves has been found.²⁹

Whether or not jaundice occurs as an early symptom depends, of course, on the site of the lesion. Thus the fact that obstructive jaundice develops early in about two thirds of the cases merely expresses the relative incidence of lesions in or near the terminal portion of the common duct. Late in the course of pancreatic cancer, jaundice becomes a frequent symptom, even when the primary lesion originates in the body or the tail, but jaundice in these cases merely indicates that the disease is advanced, with extensive metastases to the liver and to the lymph nodes surrounding the extrahepatic bile ducts.

The jaundice that occurs early is usually steadily progressive and obstructive. It is not an invariable concomitant of cancer of the head of the pancreas, however, nor is it always of a steadily progressive character.⁹ Ampullary cancers in particular may produce an inconstant icterus, for these lesions, which are situated near the orifice of the common duct, are subject to necrosis and sloughing and thereby allow an intermittent flow of bile.¹⁴ In a series of 40 cases of ampullary carcinoma, jaundice was fluctuating in 32 and intermittent in 8.¹⁰

Since jaundice occurs early in only 2 out of 3 cases of pancreatic cancer and since only 1 out of 4 patients is free from pain, it follows that painless jaundice is not a frequent characteristic of cancer of the pancreas. Berk⁶ estimates its incidence at about 20 per cent. When it does occur, it presents a symptom complex that is significant for the diagnosis of pancreatic or ampullary cancer. Perhaps because of this fact, it continues to be stressed in the literature in a way that is completely out of proportion to its incidence. In one report, for example, "painless obstructive jaundice, with diminished or absent ferments," is considered to favor the diagnosis of carcinoma of the pancreas, but the case summaries reveal that of 12 patients with cancer of the pancreas studied, 8 complained of pain.³⁰

In addition to weight loss, pain and jaundice, pancreatic cancer may give rise to a number of other

symptoms and signs, many of which, such as anorexia, weakness, edema and fever,^{12, 31} are nonspecific and do not help in reaching a diagnosis. Gastrointestinal symptoms of all types are of course prevalent, one of the most frequent being a change of bowel habits. Constipation predominates over diarrhea. It has been suggested that a normal red-cell count and the absence of occult blood in the stools of a patient who otherwise presents symptoms suggesting upper gastrointestinal cancer should make one suspicious of pancreatic neoplasm.⁶ Although this is true of many patients, others may vomit blood or may exhibit melena for one of the following reasons: the pancreatic cancer may have eroded into the stomach or duodenum, esophageal varices may have formed secondary to neoplastic invasion and thrombosis of the splenic or portal vein, hypoprothrombinemia may exist because of obstructive jaundice, and a primary lesion at the ampulla may have become ulcerated. Ulceration of ampullary carcinoma was described in 57 of 222 cases collected by Lieber, Stewart and Lund,¹⁴ and in 40 cases analyzed by Sharpe and Comfort,¹⁰ 25 patients had either tarry stools or stools containing occult blood.

"I have several times, in the wards, — pointed out to you that obliterative phlebitis is not a symptom which belongs peculiarly to cancer of the stomach, but that it is equally symptomatic of cancer of any other internal organ." These words of Trousseau³² were echoed about seventy years later by Sproul,³³ whose analysis of material at autopsy indicated that between 15 and 25 per cent of patients with most varieties of abdominal cancer suffer from venous thrombosis in the abdomen or legs. In 16 cases of cancer of the body or tail of the pancreas, however, venous thromboses were found in 9—more than twice the incidence of such thromboses with gastric cancers or with cancers in the head of the pancreas. In some cases the tendency toward thrombosis was apparently so pronounced that nonbacterial vegetations formed on the heart valves, a phenomenon that was subsequently observed in another typical case of cancer of the pancreatic tail and body.³⁴ Sproul and later Kenney,¹⁹ impressed by the frequent association of venous thromboses and neoplasms in the tail and body of the pancreas, concluded that these growths *per se* must affect the clotting mechanisms of the blood. As yet, this hypothesis has not been proved, nor has the progressive but relatively prolonged cachexia typical of cancers in the tail and body been ruled out.³⁵ Furthermore, the increased incidence of thrombosis in cancers of the body and tail of the pancreas as compared with that in those of the head may also indicate that lesions in the head produce a decreased clotting tendency, a possibility that must be considered in view of the hypoprothrombinemia that attends obstructive jaundice.

In these days of marked emphasis on psychosomatic disorders, it is well to point out that neurotic patients with pancreatic carcinoma are almost invariably suspected of having a marked psychoneurosis, partly because of the negative results obtained after the physician has exhausted his usual diagnostic armamentarium. But the situation is often more complex, for Yaskin³⁶ and subsequently others^{24, 37} reported cases of pancreatic cancer in which competent psychiatrists made diagnoses of advanced states of anxiety or depression. The association of pancreatic cancers, especially those of the body and tail, with psychiatric abnormalities does not establish a causal relation, but it does carry a warning: progressive anorexia, weight loss and back pain suggest cancer of the pancreas, regardless of whether the patient has psychiatric manifestations at the same time.

The physical signs of pancreatic cancer are manifold and depend on the location, size and spread of the tumor. A palpable mass may be discovered on rare occasions before the cancer has spread, but this finding usually indicates inoperability as much as do a rectal shelf, ascites, abdominal varices and obvious metastases to the liver, lungs or lymph nodes. A sign that may occur early and to which much interest pertains is a palpable gall bladder in patients who exhibit obstructive jaundice. This sign, of course, is linked with the name of Courvoisier, whose law, as translated literally by Ramsom,¹⁵ is as follows:

With obstruction of the common duct by stone, dilatation of the gall-bladder is rare, the organ is usually shrunken. With obstruction of other kinds, on the contrary, distention is the rule, shrinking occurs in only one twelfth of these cases.

Opinions regarding the reliability of Courvoisier's law differ widely in that palpable gall bladders have been noted by some authors^{8, 9} in less than 10 per cent of jaundiced patients with cancers in the ampulla or pancreatic head. Others, however, have palpated a distended gall bladder in 62 per cent of these cases. Reviews of the literature indicate that on the whole a distended gall bladder can be detected clinically in about half the cases of pancreatic cancer with jaundice,^{6, 14} but that at autopsy or operation enlarged and tense organs are found in about four fifths of the cases.^{6, 10, 15} The discovery of a large, relatively nontender gall bladder in a patient with obstructive jaundice may therefore be regarded as evidence for a neoplastic obstruction of the extrahepatic biliary passages, but a negative finding—that is, failure to palpate the gall bladder—is of little help in ruling out this diagnosis. A not inconsiderable number of patients have both gallstones and pancreatic cancer, a combination that makes the diagnosis extremely difficult.¹⁴

The following laboratory tests are significant in the diagnosis of pancreatic carcinoma: stool exami-

ation for excess fat and protein, determination of glucose in blood and urine, analysis of serum and duodenal contents for pancreatic enzymes and, if jaundice is present, the establishment of its obstructive character

As has been known for many years, a diffuse carcinoma involving the whole pancreas or a small lesion so situated as to block the pancreatic ducts may impair the digestion of fat and proteins, which consequently appear to excess in the feces. The stools are then light colored, greasy and bulky, the weight of the stools occasionally reaching five times normal.³⁸ In spite of the fact that steatorrhea and creatorrhea are well established findings in cancers of the pancreas, little information exists regarding the frequency of their occurrence. After reviewing the literature, Berk⁶ concluded that less than 10 per cent of patients with pancreatic cancer pass fatty stools. One must remember, however, that most series of cases are taken from hospital files, are rarely studied by the author himself, are often not suspected of having pancreatic cancer during life, and that "rarely, even in leading hospital clinics, are the stools adequately examined."³⁸ On the other hand, steatorrhea and creatorrhea occur rather late in the course of pancreatic disease,³⁹ and some patients may have fairly normal stools, even after complete pancreatic atrophy⁴⁰ or resection.⁴¹ A rough estimate indicates that a fourth of the patients with ampullary or pancreatic carcinoma pass fatty stools with a high nitrogen content, but that unless the patient is jaundiced — that is, obstruction is present in the ampullary area — steatorrhea and creatorrhea indicate advanced disease.

Precise analyses of stools are troublesome to carry out, not the least difficulty being a quantitative three-day stool collection, but if facilities are available, quantitative analyses for fat and nitrogen are of great help. Normal persons usually excrete less than 5 per cent of the fat intake and rarely pass more than 12 gm of fat in the stools a day.⁴² In pancreatic steatorrhea 30 to 50 per cent of the intake may be lost in the stools. (It should be noted that excretions of fecal fat expressed in absolute values, such as grams per day and percentage of intake, are significant, fecal fat expressed as percentage of dry weight of the stool gives a rough index but is not completely satisfactory, since the percentage of fat varies inversely with the amount of other material in the dried stool.)

Although facilities for quantitative measurement of the daily fecal fat loss may not be available, there is little excuse for not staining a stool sample with an alcoholic solution of sudan III. This stain imparts a red or orange color to fat droplets and to some crystalline and amorphous lipid material, although the orange-staining fatty-acid crystals frequently described in laboratory manuals are rarely seen. A careful study by Andersen⁴³ showed that

the amount of sudan-staining material is an excellent indication of the percentage of fat present in the stool but only a fair indication of the total fecal fat. She concludes that a negative finding (less than 2 fat droplets per low-power field) and a ++++ finding (about half the visible material stained with sudan) are highly significant. When mineral oil is used, the test is unreliable. Another important contribution made by Andersen are her observations suggesting that bacteria in the colon split neutral fats. This explains why patients with pancreatic deficiency excrete so much split fat in the stools, when one would expect the deficiency in lipase to result in a large output of unsplit, neutral fat.

Pratt³⁸ believes that pancreatic deficiency in protein digestion can be detected by the identification of meat fibers on microscopic examination of the stool. Other investigators⁴⁴ consider the presence of meat fibers less significant, since they may be found in other forms of diarrhea and since the digestion of meat is related to gastric as well as pancreatic function. The question is important, for the amount of nitrogenous material excreted in the feces provides a good means of separating pancreatogenous steatorrhea from that of sprue or pure biliary obstruction.⁴² In normal persons and in patients with nonpancreatogenous steatorrhea, the daily fecal nitrogen excretion is less than 3.0 gm, in patients with pancreatic deficiency the creatorrhea exceeds this amount.⁴⁵

Cancer of the pancreas and abnormalities in carbohydrate metabolism occur together more frequently than can be accounted for on the basis of chance. The reported figures on the coincidence of these diseases vary widely, but again the differences may depend on the criteria used in diagnosing diabetes, — glycosuria, an elevated fasting blood sugar or an impaired glucose-tolerance curve. Using the glucose-tolerance test, Berk⁶ found abnormal results in 7 out of 9 cases, but an elevated curve was found in only a fifth of the cases he collected from the literature. This ratio corresponds to the average incidence of glycosuria and fasting hyperglycemia reported by various subsequent writers, but the individual figures vary from zero⁹ to 30 per cent.⁷ The situation is analogous to that pertaining to fatty stools: evidence for diabetes increases in proportion to the effort made to uncover abnormalities of sugar metabolism.

At first glance, the association of pancreatic carcinoma and a diabetic condition seems obvious. Actually the situation is more complex. Even with extensive neoplastic replacement of acinar tissue, the islands of Langerhans may be spared.⁴⁶ ⁴⁷ So far as can be judged from the pathologic picture, consequently, many cancers of the pancreas are not diffuse enough to account for an associated diabetes. Furthermore, in many cases, the diabetes antedates the symptoms of pancreatic cancer by many years.⁴⁷ ⁴⁸ In keeping with this fact, Marble⁴⁷ found

that in 256 patients who suffered from both diabetes and cancer, pancreatic cancer, which was definitely proved in 21, accounted for 8 per cent of all carcinomas in the diabetic cases as compared with 1 or 2 per cent in the population at large. These figures suggest the possibility that diabetes is occasionally the precursor of cancer of the pancreas, rather than vice versa. Although a definite causal relation between diabetes and pancreatic cancer cannot be established, the two conditions coexist frequently enough for any suggestion of a diabetic state to intensify suspicion of pancreatic cancer if the clinical picture is otherwise suggestive.

With the development of methods for determining the concentrations of pancreatic enzymes in the blood and the duodenal contents, it was hoped that the diagnosis of pancreatic disease would be greatly facilitated. This hope has been realized only in part, for results well within the normal range may be obtained unless the cancer obstructs the pancreatic ducts or destroys more than half the pan-

Similar results can be expected in patients with tumors of the ampulla.⁵² As has been emphasized, an elevated serum lipase or amylase implies pancreatic disease,⁵² but not the type, a clear-cut dissociation, however, with a persistently high lipase and a normal amylase, suggests cancer.⁴⁹ Some cases of an obstructing ampullary lesion with initially elevated values for serum lipase may eventually display values in the low normal range, since the obstructed acinar cells atrophy or are invaded by neoplasm. A cancer of the pancreatic acini with function is rare, but such a case has apparently been observed,⁵³ since the concentrations of the serum amylase and lipase were, respectively, nearly one hundred times and ten times the normal values.

On the basis of experiments performed with dogs, Popper and his associates^{54, 55} suggested that valuable information could be obtained from serum enzyme determinations after stimulation with an intravenous injection of secretin and a subcutaneous dose of acetyl-beta-methylcholine chloride (Mecho-

TABLE 1 Data in 37 Cases of Pancreatic Cancer Reported in the Literature

AUTHOR	TOTAL NO OF CASES	SITE OF CANCER	REDUCTION IN VOLUME AND BICARBONATE SECRETION	REDUCTION IN TOTAL ENZYME OUTPUT	ICTERUS
Agren and Lagerlof ⁵⁶	7	Head, 6 Body, 1	3	4	4
Bauman and Whipple ⁵⁰	11	Head, 9 Not stated, 2	Not stated	10	7
Pollard, Miller and Brewer ⁵⁹	6	Head, 5 Tail, 1	3	3	Not stated
Friedenwald and Morrison ¹¹	8	Not stated	Not stated	5	Not stated
Diamond and Siegel ⁶⁰	3	Head, 3	2	3	3
Pratt, Brugsch and Rostler ⁶¹	2	Head, 2	2	2	2

creatic acini. Another, somewhat different, source of difficulty is the great number of methods and modifications of methods used by various investigators. Some standard methods of determining and some standard units of expressing concentrations of pancreatic enzymes must be adopted before the value of this analysis can be appraised.

Determination of the serum amylase (diastase) concentration has occasionally yielded a high figure in cases of pancreatic cancer, but on the whole not much help can be expected from this test.^{44, 49} The urine amylase content, which fluctuates more than the serum content, is even less significant.^{38, 48} Determination of serum lipase, by contrast, is of the greatest value. In the Cherry-Crandall⁶⁰ method, which is almost universally used, the lipase content of the serum is expressed as the number of cubic centimeters of 1/20 normal sodium hydroxide solution necessary to neutralize the fatty acids formed by the action of 1 cc of serum on an olive-oil substrate. Johnson and Bockus,⁵¹ who placed the upper limit of normal for this test at 10 cc, found an elevated lipase in 16 out of 30 cases of pancreatic cancer "at least once during the course of the illness." Even if 15 cc is used as the upper limit of normal, an elevated serum lipase is found in about half the cases of pancreatic cancer.^{49, 52}

lyl). If this stimulation fails to elevate the serum concentrations of amylase and lipase, the authors believe, pancreatic hypofunction may be suspected. On the other hand, elevation of the serum lipase after an intravenous injection of secretin insufficient to alter the level in a normal subject suggests obstruction of the pancreatic ducts.

The pancreatic secretion in cases of pancreatic cancer may be reduced in volume and may contain a decreased concentration of bicarbonate, amylase, trypsin and lipase. The reductions are often noticeable in the fasting secretions, but the deviation from normal is more apparent if the pancreas is stimulated with secretin or acetyl-beta-methylcholine chloride. The former has been relatively unavailable, but the results obtained with the latter should be equally if not more satisfactory, since the drug stimulates a secretion of normal volume but of increased enzyme concentration,⁵⁶ and it is stated that the enzyme output is the first to suffer in pancreatic disease.⁵⁷ Over half the cases of pancreatic cancer are reported to exhibit a decreased enzyme concentration in the duodenal juices (Table 1). Possibly a somewhat false impression of the value of the test in the early diagnosis of pancreatic cancer is given by the data, for cases with advanced disease are included. Nevertheless, analysis of the duodenal

contents for pancreatic ferments after stimulation with secretin or acetyl-beta-methylcholine chloride yields invaluable information, particularly since depression of pancreatic enzymes may precede the onset of jaundice or steatorrhea.^{39 53 62}

Scattered case reports indicate that the sedimentation rate is elevated in advanced cases of cancer of the pancreas, but this test usually gives normal results when the lesion is small and localized.^{39 53}

When a patient is icteric, it is the function of laboratory tests to determine the type and course of the jaundice. Jaundice that results from pancreatic or ampullary cancer is typically progressive, nonfluctuating and obstructive—that is, the stools remain acholic, the heavily bile-stained urine contains no urobilinogen and almost all the serum bilirubin can be quantitated with the direct van den Bergh reaction. The completeness of the obstruction produced by the usual neoplastic invasion or compression of the external biliary passages is reflected in the fecal urobilinogen content. Measured by Watson's⁶³ method, the daily fecal output of urobilinogen in patients with obstructive jaundice caused by carcinoma is less than 5 mg, in those with noncancerous jaundice of the obstructive type—caused by common-duct stones, strictures, pancreatitis or severe hepatitis—the urobilinogen output in the stools is greater. Although this test is helpful in the diagnosis of many pancreatic or ampullary cancers,⁶⁴ the results may be misleading in cases of ampullary tumors that exhibit fluctuating or even intermittent jaundice.

Since there is no method of direct x-ray study of the pancreas, the roentgenographic demonstration of tumors in this organ depends on abnormalities produced in its adjoining hollow viscera. A small intrapancreatic or a diffuse scirrhous cancer that replaces the normal tissue without concomitant enlargement of the gland may consequently go undetected in spite of painstaking radiologic examination. Large tumors may displace the stomach upward and ventrally, the descending duodenum laterally and the transverse duodenum and transverse colon downward.^{26 65} Of these deformities, a large C-shaped duodenal loop is perhaps the best known, but its interpretation is often difficult, especially in hypersthenic persons. In patients of this habitus, the stomach is usually stretched across the spine high in the epigastrium and thus exposes the whole duodenal loop, which has an appearance of enlargement.

Massive displacement of the adjoining viscera by a pancreatic cancer is a poor prognostic sign, since it suggests a large and advanced neoplasm. Smaller cancers situated in the periphery of the pancreas may, however, manifest themselves by the production of localized deformities in the gastrointestinal tract. Changes in the mucosal pattern or alterations in the finer outlines of the stomach or duodenum may appear before the cancer has invaded

the mucosa, later filling defects and evidence of ulceration may develop as the tumor extends into the lumen of the bowel. So far as the duodenum is concerned, considerable attention has been directed to the so-called "reverse figure-3" sign. As originally described by Frostberg,⁶⁶ the entire descending duodenum participates in forming such a sign, the top of the figure starting just beyond the duodenal cap, its lower pole at the beginning of the transverse duodenum and the prong in the middle of the figure pointing toward the spine in the region of the ampulla. Frostberg, who found this duodenal configuration in 1 case each of pancreatitis, of cancer of the pancreas and of cancer of the ampulla, assumed that it was produced by pressure on the medial wall of the duodenum, with relative fixation of the ampullary area. Other authors⁶⁷⁻⁶⁹ have used the reverse figure-3 sign to describe smaller lesions that at times seem to include only the lips of the papilla of Vater, the central prong of the figure being formed by the entrance of the ampulla. Both large and small configurations are sometimes observed in normal duodenum.^{26 66}

When case records of patients with pancreatic or ampullary cancer are reviewed, the incidence of gastrointestinal abnormalities as demonstrated by x-ray examination varies markedly in different series. In some, positive findings are claimed in nearly three fourths of the cases;^{17 47} others report an incidence of about 50 per cent,^{6 7} whereas still others^{5 10 16} consider abnormal roentgenologic findings unusual. Although some abnormality in the radiologic appearance of the stomach, duodenum or colon may be observed in about a third of the cases of pancreatic or ampullary cancers, the findings are diagnostic in a much smaller number, especially if indications of an early lesion are being sought.

A rather ingenious method of visualizing the pancreas was proposed by Engel and Lysholm⁷⁰ twelve years ago. This consisted of having the patient lie prone, inflating the stomach with air through a tube or by giving an effervescent mixture and then taking a lateral roentgenogram. Ideally the gas in the stomach tends to outline the dorsal aspect of this organ, and the pancreas appears as a shadow between the air-filled stomach and the lumbar vertebrae. Using this technic, Engel and Lysholm⁷⁰ and Holm⁷¹ believed that they had obtained positive results in 86 per cent of their cases of pancreatic cancer. Enlargement of the pancreas, however, must be present if positive results are to be obtained by this method, and false-positive reactions may occur in short, thickset persons who have excess retroperitoneal fat.^{70 72}

In patients who have a tube in the common duct after choledochostomy, cholangiography occasionally reveals the presence of a pancreatic cancer by demonstrating a dilated common duct that is cut off rather abruptly at its distal end.^{73 74} If the

head of the pancreas is free of disease, pancreatic reflux sometimes complicates cholangiography, but apparently no tumors of the body or tail have been discovered by this method.⁷⁶ Peroral catheterization of the ampulla of Vater has been tried in cadavers, but must be difficult in patients living.⁷⁶ A method that may hold some hope for the early identification of lesions in the pancreatic head or the ampulla is the nonsurgical cholangiography developed by Royer and Solari.⁷⁷ By this method, the gall bladder and bile ducts are injected with radio-opaque material through a peritoneoscope. Demonstration of an enlarged gall bladder, of dilated biliary passages and of the obstructed end of the common duct is perhaps feasible by this technic in patients suffering from pancreatic or ampullary cancer.

SUMMARY

Improved surgical methods of removing tumors of the pancreas or ampulla of Vater demand early diagnosis of these diseases. In many cases this goal cannot be achieved with present knowledge and technic. In others, the fatal delay that withholds a possible surgical cure from the patient can be avoided by an appreciation of the following facts:

Almost all patients with cancer of the pancreas lose weight rapidly and progressively. Many of them have a boring upper abdominal and back pain unrelated to any gastrointestinal function. Many others have obstructive jaundice. The combination of any two of these symptoms is highly indicative of pancreatic cancer, particularly if the patient is a man over forty years of age.

A palpable, nontender gall bladder in a jaundiced patient is suggestive of cancer in or near the head of the pancreas. The absence of this sign does not exclude pancreatic cancer.

Laboratory tests, as a rule, are helpful when positive and of little significance when negative. Particularly suggestive are the following: a persistent obstructive jaundice, with acholic stools and no urobilinogen in the urine, a high serum lipase and a normal serum amylase, absent or greatly diminished enzymes in the pancreatic secretion stimulated by secretin or acetyl-beta-methylcholine chloride, and stools containing an excess of both fat and nitrogen.

Less significant, but consistent with the diagnosis of pancreatic cancer, are hyperglycemia, glycosuria or impaired glucose tolerance and an elevated sedimentation rate.

At present, the roentgenologic diagnosis of pancreatic cancer depends principally on deformities produced in adjoining hollow viscera. Greater use of new technics may increase the usefulness of the x-ray in the diagnosis.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., Editor

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CASE 32441

PRESENTATION OF CASE

A forty-nine-year-old salesman entered the hospital because of severe dyspnea.

At approximately twenty years of age, the patient developed a chancre for which he received intravenous injections of an "antisyphilitic drug" over the course of a year. He was well until three years before admission, when a left Bell's palsy occurred a day following exposure to cold air while he was sleeping outdoors. At about the same time he began to experience shooting pains in the lower back and at times down the legs and arms. Two months before admission he was awakened by a severe precordial pain radiating to the left shoulder. He sweated, felt suffocated and feared impending death. Partial relief was obtained from an injection given by a physician. The patient coughed blood-streaked sputum for four days. There had been no previous cardiac or pulmonary symptoms, although the patient was known to have a systolic

blood pressure of 170. At the end of four days he entered the Emergency Ward, where a Grade II apical systolic and a questionable aortic diastolic murmur were heard. There was no tenderness over the leg vessels. The pupils were fixed, the left one being oval in a perpendicular plane. An x-ray film of the chest was negative except for calcification of the aorta. The cardiac consultant described faint systolic and early, blowing diastolic murmurs at the aortic areas, as well as a presystolic murmur at the apex. An electrocardiogram showed inverted T_1 , T_{CF_1} and T_{CF_2} , and upright T_2 and T_{CF_2} . Left-axis deviation was present, with a PR interval of 0.14 second. The blood Hinton reaction was positive; the blood Wassermann reaction was negative, and the spinal-fluid Hinton and Wassermann tests were positive; the gold-sol curve was 442210000. The precordial pain cleared spontaneously, and the patient was discharged on the fourth day to the Out Patient Department, where he was given four 0.2-gm intramuscular doses of bismuth at weekly intervals for a month. The facial palsy appeared worse at the end of this time, and severe attacks of nocturnal dyspnea and non-radiating precordial oppression suddenly began. Later the patient became dyspneic and orthopneic during the day. A week before admission, after three weeks of severe dyspnea, the voice became hoarse.

On examination the patient was orthopneic and hoarse. There was a blowing, Grade III diastolic murmur in the aortic area and down the left sternal border and a Grade II diastolic mitral murmur. There were dullness, decreased breath sounds and sticky rales at both bases, more on the left than on

the right. The liver edge extended 5 cm below the costal margin. There was slight pitting edema of the ankles. The pupils were fixed to light but reacted to accommodation. A facial paralysis was present.

The temperature was 100°F, the pulse 100, and the respirations 21. The blood pressure was 125 systolic, 25 diastolic.

Examination of the blood showed a red-cell count of 5,170,000, with 12.9 gm of hemoglobin per 100 cc, and a white-cell count of 10,400, with a normal differential. The urine was normal.

In the hospital the patient was restless and dyspneic and complained of substernal burning. On the morning after admission he became extremely restless and then manic, he clutched wildly at his chest, complained of precordial pain and died in a few minutes.

DIFFERENTIAL DIAGNOSIS

DR EDWARD F BLAND The first and foremost feature of this case is syphilis. The initial infection began twenty-nine years before the final disintegration. The early treatment was inadequate by present standards, and in due course the patient appears to have developed active neurosyphilis and almost certainly fatal cardiovascular syphilis. The first clinical feature of some interest is centered around the possibility of neurosyphilis. In addition to the positive serologic findings and abnormal gold-sol curve, he had typical Argyll-Robertson pupils. Furthermore, the spinal-fluid Wassermann reaction was positive. In this connection, one would like to know the spinal-fluid cell count and the protein content, as well as the state of the peripheral reflexes.

DR TRACY B MALLORY The total protein was 24 mg per 100 cc. There is no record of the cell count.

DR BLAND That does not help much. I expected that it might be elevated. Nevertheless, in view of the shooting pain three years before entry and the abnormal findings in the spinal fluid, I suspect that the patient had active late neurosyphilis.

How are we to interpret the seventh-nerve palsy? Isolated seventh-nerve palsy is rarely due to syphilis. In this case I attribute it to peripheral neuritis following exposure to cold.

Then, we come to his admission to the Emergency Ward, which followed the sudden onset of precordial pain that radiated to the left shoulder for four days, and the raising of bloody sputum. We do not know whether there was fever, what was heard in the lungs, or whether breathing was painful. We are told simply that the patient had pain, which was presumably imperfectly relieved by morphine. What could this have been? A pulmonary infarct, of course, is the first thing that comes to mind. The radiation of the pain is consistent, but it would

be helpful to know some of the other clinical details mentioned above.

To what else could it have been due? A coronary occlusion? The electrocardiogram is consistent with that diagnosis. It could also have been due to uncomplicated acute pulmonary congestion from left ventricular failure, or to congestion behind a marked mitral stenosis. It could also have been due to an infection or an expanding (or leaking) aneurysm. I favor pulmonary infarction as the most probable explanation for this illness. Furthermore, I should like to know what the blood pressure was at that time, in view of the abnormal blood-pressure determination recorded a month later. The electrocardiogram was definitely abnormal.

DR MALLORY The blood pressure was 120 systolic, 20 diastolic.

DR BLAND That is a wide pulse pressure and not significantly different from that on the second admission. Therefore, the patient had free aortic regurgitation in spite of the uncertainty about the murmurs. This illness with pain and hemoptysis must not have been taken too seriously, because he remained only four days in the hospital.

Then we come to the physical signs, which were largely limited to the heart. He had a wide pulse pressure, and one observer thought that he had aortic regurgitation. In addition, the characteristic murmur of mitral stenosis was described. That can be present in the absence of mitral stenosis if there is marked dilatation of the heart secondary to free aortic regurgitation. As the murmur is described, however, one must seriously consider the possibility of rheumatic mitral-valve involvement. The electrocardiogram was abnormal but not diagnostic and not particularly suggestive of a recent myocardial infarct. The abnormal findings could have been due to left ventricular strain in the presence of the wide pulse pressure and the evidence of aortic regurgitation. This explanation seems most probable, with perhaps the added effect of constricted coronary ostia. There was not a later tracing by any chance?

DR MALLORY No. Since the first admission was simply to the Emergency Ward, there was no complete workup.

DR BLAND The patient did fairly well. He went home and had four injections of bismuth. Thereafter he rapidly became worse and in the course of a month returned in a serious state, with acute and rapidly progressive heart failure. Until I knew what the blood pressure was at the first admission, — it was not referred to in the original record, — I was inclined to put some emphasis on the apparently striking increase in the aortic regurgitation within a month. The question is, Did the treatment do him any harm? He had had no penicillin. He had had no arsenic. These are the two drugs whose administration might seriously be questioned in the

presence of advanced cardiovascular syphilis with heart failure. Bismuth does not ordinarily cause a Jarisch-Herxheimer reaction by rapid resolution of syphilitic inflammatory tissue. It can cause slow resolution of a gumma, but we have no reason to think that this man had gummatous lesions. At this point we would like to examine the x-ray films.

DR. JAMES R. LINGLEY: I am sorry. The x-ray films have been destroyed.

DR. BLAND: I should have liked to know whether the calcification was limited to the first portion of the aorta. The roentgenologists repeatedly call our attention to the fact that this finding is an important clue to the presence of syphilitic aortitis. Is that correct, Dr. Lingley?

DR. LINGLEY: Yes.

DR. BLAND: I should also have liked to know the size of the aorta and of the heart. Presumably both were dilated. The terminal rapid disintegration and heart failure is further evidence consistent with cardiovascular syphilis. Therefore, I cannot seriously consider any other diagnosis. I could discuss at length the various details of what may have happened at the end. I shall conclude, however, that the patient had neurosyphilis, which was late and possibly active, and that he had cardiovascular syphilis, aortitis and free aortic regurgitation. It is likely that the coronary ostia were constricted by the syphilitic process. I am bothered by the apical diastolic murmur, which, as described in the record, is characteristic of mitral stenosis. The patient died primarily of congestive heart failure.

CLINICAL DIAGNOSES

Syphilitic aortitis
Aortic regurgitation
Myocardial infarction

DR. BLAND'S DIAGNOSES

Cardiovascular syphilis, with aortitis and aortic regurgitation
Congestive heart failure
Neurosyphilis, late, active
Mitral stenosis?

ANATOMICAL DIAGNOSES

Syphilitic aortitis, with aortic insufficiency
Cardiac hypertrophy and dilatation, predominantly of left side
Infarct of heart
Pulmonary edema, massive
Hydrothorax
Pulmonary tuberculosis

PATHOLOGICAL DISCUSSION

DR. MALLORY: The autopsy on this man showed characteristic syphilitic heart disease. The valvular involvement was limited to the aorta. The cusps were separated at the commissures for a distance of 3 or 4 mm. The individual cusps were

thickened, sclerosed and contracted. The aorta was markedly sclerotic, diffusely dilated, wrinkled and scarred in spots between the atheromatous plaques. The entire process was most marked in the thoracic portion of the aorta, diminishing as one proceeded toward the abdominal portion, which is characteristic of syphilis and in contrast to ordinary arteriosclerosis. The coronary ostia, especially that of the left coronary artery, were definitely narrowed by the aortic process. Beyond their mouths they were relatively free from atheroma, nevertheless, there was a large area of scarring at the base of the left ventricle, where the muscle was thinned to a width of only 3 mm. The gross appearance was quite consistent with an ordinary cardiac infarct. There was nothing in the microscopic sections to make one change that diagnosis — nothing, for instance, to suggest a gumma of the myocardium, which is occasionally seen. The lungs showed extensive tuberculous scars at both apices surrounded by focal emphysema, a marked grade of chronic passive congestion and acute terminal pulmonary edema. They weighed over 2200 gm. at the time of autopsy and exuded turbid fluid on the slightest pressure. I cannot give the answer about the central-nervous-system involvement. We did not have permission to examine the brain, and the small section of the cord that was removed by the anterior approach did not show anything. I do not believe that that rules out the possibility of tabes.

CASE 32442

PRESENTATION OF CASE

A fifty-six-year-old woman entered the hospital because of a lump under the left breast.

The patient was apparently well until two years before entry, when she first noticed a small nontender swelling on the chest wall below the lateral portion of the left breast. This swelling increased slowly at first but more rapidly during the following year. It was never painful or inflamed, but several weeks before entry, the patient began to have occasional twinges of pain posterior to the mass.

The patient had had the usual diseases of childhood. Fifteen years before entry she had had typhoid fever, which cleared after four weeks without complications. Four years before entry the urine was reported to contain albumin. Three and a half years before entry she passed about 25 cc of bright-red blood by rectum, a similar episode occurred two weeks before entry. A year before entry she had an attack of bronchitis requiring bed rest for a week. Six months later, the patient noticed slight exertional dyspnea and occasional episodes of tachycardia, but there was no orthopnea, ankle edema, cough or chest pain. During this period she also had frequency and nocturia (five or six times). There had been no recent weight loss.

The patient's mother, sister and brother had died of tuberculosis, and the patient had attended her brother during his final illness twenty years before entry

Physical examination showed an obese woman in no distress. Over the chest wall anteriorly beneath the left breast, a hard, rounded mass measuring 4 by 6 cm was firmly attached to the eighth and ninth ribs and moved with them. It had no connection with the breast. Firm pressure over the mass caused a "drawing sensation," with a slight ache radiating back along the ribs. The breasts were normal. The lungs were clear. The heart was normal except for a Grade I systolic murmur at the apex.

The temperature, pulse and respirations were normal. The blood pressure was 210 systolic, 110 diastolic.

The white-cell count was 5500, and the hemoglobin 12.5 gm. The total protein was 7.5 gm., and the fasting blood sugar 84 mg. per 100 cc. A blood Hinton test was positive. Examination of the urine was negative.

An x-ray film of the chest showed a 6-cm. soft-tissue mass overlying the anterior extremity of the left eighth rib. There was some bone destruction and thickening of the periosteum along the inner margin. The lungs were clear. An electrocardiogram was consistent with coronary disease.

On the seventh hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR RICHARD H. WALLACE: It is unusual in a case of this sort — a tumor of the chest wall — to have so many hints in the history that might lead to a diagnosis.

I believe that the hypertension and heart disease had nothing to do with the mass in the chest wall. The patient had typhoid fever fifteen years before admission. It is possible, many years after typhoid fever, to have a rib infection from the typhoid bacillus, although a lesion of that sort is apt to be tender and is not likely to cause a tumor of this size and consistence. The second point is that on two occasions blood was passed by rectum, suggesting that three years previously the patient had had a primary cancer of the intestinal tract. But there is no further mention of the passage of blood, and no rectal examination, proctoscopic examination or barium study was done, so that the incident was presumably considered irrelevant.

The patient had had bronchitis and had certainly been exposed to tuberculosis, since her mother, brother and sister had died of it, and it is stated that she had taken care of her brother in his final illness, so that tuberculosis should be considered.

The statement that the blood Hinton reaction was positive immediately makes one think of gumma, which is not rare in the chest wall. It usually occurs,

however, along the border of the sternum. Perhaps the x-ray films will be helpful.

DR JAMES R. LINGLEY: This film gives an excellent view of the mass, which extends well out into the soft tissues, but there is no edema of the overlying soft tissues. The mass is smooth and sharply defined, with destruction of the anterior portion of the rib at the costochondral junction. There is also slight expansion and some new-bone formation.

DR WALLACE: Would you say that the tumor probably had its origin in the rib or in the soft parts?

DR LINGLEY: I think that the expansion of the rib is in favor of the former location.

DR WALLACE: There is nothing to suggest inflammation or osteomyelitis. Tuberculosis, of course, must be considered. The chest plate was negative, so that there was apparently no active pulmonary disease. The costochondral margin is a fairly frequent site for tuberculosis. I believe, however, that it is extremely unlikely in this case. Although the tumor did not have the appearance of a gumma, it certainly could have been, and I do not believe that we can definitely rule out such a diagnosis.

We therefore have the possibility of tumors, benign or malignant, that have their origin in bone. In considering the various cells from which such tumors arise, on the marrow side these cells may give rise to myeloma, which is usually multiple, of course, and with this duration extremely unlikely to be still localized. In addition, myeloma shows marked bone destruction, and one would not expect a sizable soft-part tumor. The reticuloendothelial cells presumably give rise to a Ewing tumor, which is also primarily a destructive lesion and could hardly cause a large, hard, soft-part tumor with so little destruction in the rib. The cartilage cells might result in either a chondroma or a chondrosarcoma. This lesion is at the costochondral junction, but it does not have the multilocular appearance or the marked expansion that is ordinarily seen with cartilaginous tumors. The osteoblasts, of course, give rise to osteoma, but in that situation one would not expect destruction. Could this have been osteogenic sarcoma? I think that it is extremely unlikely. The patient, who was over fifty years old, was not in the proper age group, and it is extremely rare to have osteogenic sarcoma in the rib — most of these tumors occur in the ends of the long bones. Could this have arisen from the osteoclastic cells, thus producing a giant-cell tumor? It had none of the characteristics of a giant-cell tumor on x-ray examination. Lymphoma must always be considered, and in the chest wall reticulum-cell sarcoma especially has to be thought of. I cannot rule it out. Many of the rarer tumors, such as the hemangioma, the eosinophilic granuloma and the plasma-cell tumor, should also be mentioned.

Could this have been a metastatic tumor? We have no lead for the site of the primary tumor, and

tastatic lesions are ordinarily punched out, such a large, soft-part tumor is unusual, although it is occasionally seen following carcinoma of the breast. The breast had not been entirely normal, I think. I might seriously consider that diagnosis. On the other hand, about once a year we see metastatic tumor from carcinoma of the breast in which the breasts are completely normal to palpation, and I call one or two cases in which the pathologist had difficulty in finding the minute primary tumor that had given rise to widespread metastases.

The question then comes up whether this tumor originated outside the rib. This seems unlikely because of the x-ray findings.

I neglected to mention another definite possibility—a periosteal fibrosarcoma originating near the edge of the rib and involving it secondarily.

One other extremely rare tumor that is practically never seen is a myoblastoma. This ordinarily has its origin in the tongue in about half the reported cases, but it can occur anywhere in striated muscle. At Pondville Hospital we recently had 2 cases. One had its origin in the deltoid muscle, and the other in the muscles in the palm of the hand. In both cases the tumor was removed locally, and both patients died within eighteen months from widespread osseous metastases without local recurrence. The decision about the nature of the tumor is a matter of speculation, and it finally becomes necessary to do either a biopsy or an excision of the tumor before the real diagnosis becomes evident. But in this particular case I do not believe that tuberculosis or gumma can be ruled out. My first guess, and it is only a guess, is reticulum-cell sarcoma, and the second, fibrosarcoma, probably periosteal in origin.

DR. TRACY B. MALLORY: Dr. Lingley, would you care to make a diagnosis on the x-ray findings alone?

DR. LINGLEY: As Dr. Wallace says, it is a guess, and we can tell definitely only on pathological examination. In this case the point of origin was somewhat in favor of a cartilaginous tumor. I would put chondrosarcoma as my first choice.

CLINICAL DIAGNOSIS

Chondroma of rib

DR. WALLACE'S DIAGNOSIS

Reticulum-cell sarcoma of rib

ANATOMICAL DIAGNOSIS

Chondroma of eighth costal cartilage

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Herrera, will you describe the operative findings?

DR. RODOLFO E. HERRERA: We certainly did not believe that we could rule out a malignant lesion and for that reason decided on radical surgery, which was done at the first opportunity, with the danger of recurrence in mind. We knew that rib tumors have been known to spread through the marrow and to recur at different parts of the rib. Consequently, the chest was entered through the seventh intercostal space, and the tumor was explored from within the pleural cavity. It seemed to arise from the costochondral junction. The seventh and eighth interspaces were occupied by the tumor, and segments of the seventh and ninth ribs were removed by block excision and the eighth rib in toto, with part of the costal arch.

DR. MALLORY: The resected specimen showed a large cartilaginous tumor that evidently arose from the rib cartilage. As in most of these tumors, it looked essentially benign from the histologic point of view. We know, however, that these tumors must be treated with a good deal of caution. We have had one case, which Dr. Herrera mentioned, in which there was extension backward for a considerable distance through the rib. On the other hand, that was a single case. To my mind, the great danger in a case of this type is that certain cartilaginous tumors, in particular those in the rib and symphysis pubis, implant with the most extraordinary facility. It seems as if one tumor cell dropped in the wound almost inevitably grows and is followed by recurrence. We have had a number of such cases. In one, local resection was done, recurrence developed, the parietal pleura was removed, recurrence again developed on the visceral pleura, then some cells dropped down on the surface of the diaphragm, the diaphragm was resected and so on. In spite of the histologically benign appearance and the slight probability of metastases, these are cases that should be radically excised at the first operation, as was done in this case.

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GREATER BOSTON COMMUNITY FUND

THE Greater Boston Community Fund will conduct its campaign for funds to support its Red Feather Services during the first part of November. The Physicians' Division will solicit during the period October 28 to November 15, its quota being \$23,000. The organization of the division is as follows: group chairman, Dr. John P. Monks; group vice-chairmen, Drs. Richard Stetson and George Sturgis; group committeemen, Drs. Archie Abrams, Myles Baker, Marshall Bartlett, Eugene Eppinger, Robert Joplin, Helen Pittman, Vernon Williams, Arthur Pier, Thomas Quigley, Gordon Donaldson, T. Cannon Eley, Paul Chandler, Charles Shedd, Walter Garrey and

Benjamin Tenney. In addition, some ninety physicians will act as solicitors.

Everyone is well aware of the time and effort that many physicians are constantly giving without recompense to charitable institutions. On the other hand, contributions to the Fund represent their support as citizens of the hospitals and social agencies of this community. The drive is a vivid example of a democracy working at its best.

THE OUTLOOK FOR INFLUENZA

IN a recent paper the Commission on Acute Respiratory Diseases¹ formulated a theory concerning the periodicity of influenza. It is based on published data concerning excess annual death rates from influenza and pneumonia since 1920 and on more precise information concerning the occurrence of epidemics of influenza A and B since 1932.

According to these workers, the sixteen widespread epidemics of influenza that occurred in the United States between 1920 and 1944 can be accounted for on the basis of two specific recurrent infections. Influenza A appears to have a cycle of two or three years, and influenza B a cycle of four to six years. They claim that no other influenza viruses have caused *widespread* epidemics in this country during the past twenty-five years. On the basis of this formulation, the probability of occurrence of future epidemics has been forecast within certain time limits, although exact predictions are not possible.

Specifically, the experience with the presumptive epidemics of influenza B is limited because the cycle is longer than that with influenza A and only a small number of past observations are reliable. The theory offered by the commission called for a widespread epidemic before the summer of 1946. At the time when the paper was written, there had been numerous small outbreaks of this infection that might have represented a return of influenza B five years after the previous epidemic, and there was insufficient evidence to indicate that this disease had caused an epidemic in a true sense. Only slight increases in the gross admission rates for respiratory diseases had occurred in the whole United States Army in the continental United States, although small outbreaks of influenza B occurred in certain

uts An influenza epidemic, however, occurred ward the end of 1945 that was roughly comparable in extent to the epidemic of influenza A that occurred in December, 1943.² For the country as a whole a rise in the occurrence of influenza began about the middle of November and reached peak during the week ending December 22, with definite falling off in the next two weeks. This epidemic, which involved nearly all geographic areas of the United States and also occurred in other countries, was definitely identified as being due to influenza B in all areas.

It was found that in the past twenty-seven years, even of the eleven epidemics of presumptive influenza A occurred at an interval of two years and that the remaining four had a three-year interval. On the basis of that experience, there was more than an even chance that influenza A would reappear during the winter of 1945-1946. If influenza failed to occur in that season, the probability that it would appear in the following winter was even greater.

Influenza A was identified in isolated cases during and after the epidemic of influenza B that occurred last December. Small isolated outbreaks were recognized, but no definite epidemic of influenza A occurred. If the theory proposed by the commission is correct, the occurrence of an epidemic of influenza A during the coming fall and winter is almost a certainty. Since the recognized epidemics of influenza A and B in New England have occurred during December or January, an epidemic of influenza A may be expected during those months.

The etiology of the great pandemic of 1918 is not known. Predictions regarding the future occurrence of such a pandemic, if it was caused by an agent other than the virus of influenza A or B, cannot, therefore, be made at the present time.

Considerable information has been accumulated in recent years concerning preventive vaccines against influenza-virus infections, and the subject matter has been given considerable publicity both in the lay press and in the literature distributed by pharmaceutical firms. Physicians will have considerable difficulty in deciding whether or not such a vaccine should be given to any individual or

group. In arriving at a decision, the known facts concerning the available vaccines, their efficacy and the untoward effects to be expected should be taken into consideration.

The influenza vaccines now available are prepared from fertile hens' eggs. After a stated period of incubation the eggs are inoculated with living influenza virus, which is then allowed to grow in the eggs—usually for two days. The allantoic fluid from these embryonated eggs is then harvested, and the virus contained in this fluid is concentrated by one of a number of methods and subsequently inactivated either by formalin or by other means, a preservative being added. The present vaccines usually contain about equal quantities of influenza A and B viruses, together with a certain amount of egg protein.

Influenza vaccines are now being marketed by several of the leading manufacturers of biologicals in this country. Their products are recommended for subcutaneous injection. The dose is a single injection of 1 cc for adults, and two doses of 0.5 cc each given a week apart are recommended for children. For batches of vaccine that produce excessive local or systemic reactions, the dose recommended for children should be used in adults as well.

The optimum protection to be expected from this vaccine, which is achieved about two weeks after the first injection, corresponds to the time of the maximum rise of antibody. Little if any protection may be expected within the first week after vaccination. The protection lasts at least three or four months and probably as long as a year or more. Its efficacy in protecting against both influenza A and B has already been fairly well established. The first opportunity to prove the effectiveness of these vaccines in the prevention of influenza B occurred last year. The reports indicate that influenza B was about ten times as frequent in unvaccinated persons as in those who were protected by the vaccine given in the manner suggested.³ The results in influenza A as observed during the epidemic of 1943-1944 were not quite so good but point to a considerable degree of protection from the vaccine.⁴ Generally speaking, the incidence of influenza in unvaccinated persons was two to six times, averaging about three times, as great as that in vaccinated

persons of comparable groups. The observations at that time were not all done under the most favorable conditions, and some were undertaken within too brief a period before the peak of the epidemic. Better results can probably be expected with the vaccines presently available if they are used under more favorable conditions and at a sufficient interval prior to the expected occurrence of an epidemic.

Reactions to the vaccine are of two types. One is related to sensitivity to egg protein and may be anything from mild urticaria to severe anaphylactic shock. The sensitization of persons so that they later develop allergic reactions from the injection of vaccine containing egg protein or from the ingestion of egg protein is a possibility, although sensitization of the latter type is probably rare. The second type of reaction is one related to the virus content of the vaccine. Symptoms simulating those of influenza may occur but are usually mild, of short duration and not incapacitating. They attest the efficacy of the virus and, when they occur, offer the best evidence that protection will be afforded. These reactions vary considerably with different batches of vaccine and are more frequent when the full dose is given in a single injection.

It should be borne in mind that the common cold and its complications are not prevented by the use of influenza vaccines, nor is protection afforded against bacterial infections such as streptococcal sore throat or against virus infections other than those caused by influenza.

In general, vaccination against influenza, if undertaken, should be done in the New England area during November or immediately on the first occurrence of typical cases of this disease. In the latter event, less protection may be afforded and those already exposed or who come in contact with the infection soon after inoculation may obtain no protection. Vaccination against influenza is not recommended in allergic persons unless there are special reasons for protecting them and unless it is known that they are not specifically sensitive to egg protein. Skin tests with diluted vaccine may be employed to test for such a sensitivity if vaccination is contemplated. Case histories should be obtained concerning sensitivity to egg protein and also concerning previous vaccination with materials that might contain egg protein. Vaccines against

influenza, yellow fever and typhus fever were widely employed, particularly the last, among the armed forces that operated in North Africa and in the Mediterranean Theater, and all of them contained egg protein.

Vaccination is desirable in persons who have previously had severe experiences with influenza and its complications. It may also be recommended for those who are prone to recurrent attacks of upper or lower respiratory-tract infections that persist for a long time after attacks of influenza or the common cold. Large-scale immunization against influenza is recommended among groups in which it is important to minimize the occurrence of absenteeism during the period when epidemic influenza is likely to occur. In department stores, for example, the largest volume of business is transacted in the season when influenza epidemics usually occur. Certain industries that are geared to maximum production at these times might also be hard hit by an epidemic of influenza. In colleges and technical schools, particularly now that they have accelerated programs and much overcrowding, the occurrence of influenza might put the programs entirely out of gear. Under such conditions, large-scale vaccination may be highly desirable, but care should be taken to avoid the inclusion of persons in whom reactions might prove serious.

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MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	November 1	Albert H. Brewster
Salem	November 4	Paul W. Hugenberger
Haverhill	November 6	William T. Green
Gardner (Worcester subclinic)	November 12	John W. O'Meara
Brockton	November 14	George W. Van Gorder
Worcester	November 15	John W. O'Meara
Pittsfield	November 18	Frank A. Slowick
Springfield	November 19	Garry deN. Hough
Fall River	November 25	David S. Grice
Hyannis	November 21	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments.

(Notices on page xv)

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ENDOMETRIOSIS*

Two Hundred Cases Considered from the Viewpoint of the Practitioner

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WORCESTER, MASSACHUSETTS

ENDOMETRIOSIS is a frequent, not a rare, disease. In a recent test period, controlled to the extent that during it all the clinic's operations were done by one operator, there were among the female patients 78 cases of acute appendicitis and 107 cases of microscopically verified endometriosis.

The natural course of this disease is from various stages of severe pain through dyspareunia and sterility, with all the marital disharmonies attendant on those complications, to pelvic invalidism. Endometriosis, however, is one of the few diseases with proportionately serious results for which there is a specific treatment—castration. Less radical therapy is effective if the diagnosis is made even moderately early.

Unfortunately the diagnosis is oftener missed than made. Of the last 200 patients in this clinic with external endometriosis,—to which this paper is limited,—most of whom had previously been examined by one or more physicians and several of whom had been explored, only 6 entered with a diagnosis of endometriosis. No other disease of comparable frequency and severity has had, in our own experience, so low a diagnostic index. Yet the means of diagnosis are at hand. Endometriosis has a cardinal symptom, a pathognomonic sign and an unmistakable gross appearance. Also, it occurs in a sharply limited group of the population.

The missed diagnosis is not a phenomenon peculiar to New England. Nor is it the fault of the practitioner. Despite the excellent reports on endometriosis, we have found no definite description of what we believe to be its fundamental clinical syndrome. Furthermore, there is a widespread assumption that the condition is the private property of the gynecologist. This is unfortunate because endometriosis, like pregnancy, is encountered by all physicians.

PATHOLOGY

External endometriosis is a growth of endometrium anywhere except where it belongs, in the lining of the uterine cavity, the word "growth" should be emphasized. Endometriosis closely resembles cancer. The cells are more differentiated, but it has the clinical attributes of cancer—speedy growth, spread, invasion and metastasis. Cytologically it is benign, otherwise it is cancer, but a cancer against which there is a specific treatment.

This growth, being endometrium, menstruates. The usual structural unit is an endometrial-walled cyst that menstruates into its own lumen. When the menstrual fluid meets peritoneum, it causes local chemical peritonitis. The cyst wall itself, growing centrifugally, invades the host. Invasion is opposed by growth of fibrous tissue varying in degree with the host.

When the growth occurs in an ovary there is least fibrous counterattack, the cyst enlarges rapidly and tends to perforate because it presumably becomes distended with each period. Blowout can occur, usually immediately before or early in menstruation, and produces a syndrome varying in intensity from that of mild appendicitis to that of ruptured tubal pregnancy. Seepage, as opposed to blowout, for the most part causes only an unusually painful period. Seeping menstrual fluid plasters the ovary first to the broad ligament and later to any contiguous area, with characteristic dense, cancerlike adhesions. Month after month, swellings, new seepages and new adhesions build up the so-called "chocolate cyst" of the usual illustration. It is unfortunate that so advanced a stage is the trademark of the disease. Earlier lesions are recognizable (Fig 1).

In addition to the ovary, the pelvic peritoneum, visceral or parietal, is invaded either directly or by the droppings from an ovarian endometrioma. Here the lesion eventually becomes a so-called "blueberry spot" (Figs 2 and 3).

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The blueberry spot ordinarily does not exceed a few millimeters, but the surrounding fibrosis may be 1 or 2 cm in diameter. The fibrosis spreads both in the host tissue and, through adhesion, to adjacent tissues. Octopuslike tentacles of endometrial tissue invade the fibrosis, and the lesion shows radiating stellate lines of contraction as if pulling neighboring tissues toward itself.

Figure 3, which shows endometriotic adhesions compared with those of chronic pelvic inflammation, demonstrates the difference between the thin, sheet-like, stretching adhesions of old inflammatory disease and the solid, stellate, puckering tentacles of active endometriosis. The adhesion of the inflammation, a protective mechanism whose work is done, yields to environment and weakens and stretches. The new growth invades the environs, clawing them to itself.

Blueberry spots tend to occur in groups, to coalesce and, with their fibrosis, to build up the cancerlike nodules that are the pathognomonic sign of endometriosis. Such conglomerate tumors cause extensive distortion or, in the sigmoid, stricture.

The densely adherent tumors and the intestinal involvement of late endometriosis may cause unusual difficulty for the surgeon and consequent danger for the patient. Despite the fact that all endometriosis, with the possible exception of that in more advanced sigmoidal strictures,¹ regresses after removal of the ovaries, merely reaching the ovaries to remove them may be dangerously difficult. It is fair to say that endometriosis is a disease that progresses at variable rates but in the direction of death until arrested by the menopause.

We have begun to recognize what we believe to be earlier forms of endometriosis than any of those described above. There are also less frequent forms, such as endosalpingiosis² and the debatable lesions described by Goodall,³ all of which are beyond the scope of this paper.

Endometriosis may appear in the appendix, appendix stumps, laparotomy scars, the cervix, the bladder mucosa, the vaginal wall, along the ureter, hernial sacs, the groin, the vulva, the umbilicus, the small intestine, the abdominal and mediastinal lymph nodes and probably the lung, biceps muscle and forearm.

Internal endometriosis (adenomyosis, adenomyoma) is probably a different disease.

DIAGNOSIS

Endometriosis tends to occur in childless women, in whom pelvic symptoms are likely to be ascribed to neurosis. The variety of places in which lesions occur and the triple action of the disease (as neoplasm, chemical irritant and presumptive hormone manufacturer) make almost any symptom possible. Also, endometriosis often accompanies other symptom-producing pelvic diseases, especially fibroids. A basic syndrome, however, can probably be identified

in spite of all the adventitious symptoms. The picture has three parts: a cardinal symptom, a pathognomonic sign and a specialized susceptibility.

Cardinal Symptom

In our experience increasing dysmenorrhea is almost always present, provided the disease causes any symptoms. One hesitates to call the pain dysmenorrhea, which suggests cramps. This pain may be a cramp but it may also be an ache in the left lower quadrant, an acute stab near the appendix, a soreness in the rectum or a discomfort in the back. It may be sharply localized, or it may radiate to the sacrum or thigh. The nature and location of the pain are not important. What is significant is its relation to menstruation. This relation may vary usually, the pain and the period are synchronous, but occasionally the pain precedes or follows the period, in 1 patient the pain accompanied ovulation rather than flow.

Of course, many lesions cause dysmenorrhea. The criterion of endometriotic pain is *increase*. Increasing dysmenorrhea is not the same as acquired dysmenorrhea. The pain of endometriosis may be acquired — that is, it may start after previously painless periods. Or it may be an increase of existing pain. In either event the increase continues and cumulates. Eventually pains meet across the month, and there is no longer intermenstrual remission but only menstrual exacerbation. Contrariwise, the pain of old pelvic inflammation may decrease at menstruation, possibly from hyperemia.

The severity of the pain is no index of the extent of the lesion. One of the puzzles of the disease is the patient with severe pain but slight lesion, or vice versa. By and large, the pain is more consistent with peritoneal lesions than with those limited to the ovaries. The likeliest to escape diagnosis is the endometrioma, that slowly builds up within an ovary, without seepage and without peritoneal implant, and bursts without warning. One should be wary of appendicitis that occurs on the day preceding menstruation.

What proportion of patients who have increasing dysmenorrhea do not have endometriosis? Unfortunately the clinic lacks a symptom index, so that the answer cannot be given in numbers. Our impression is that the fraction is small.

The history of increasing dysmenorrhea probably bears some relation to the pessimism of many authors about diagnosis. Although appraised as the chief and characteristic symptom of the disease as early as 1929 by King and Fiddes,⁴ its significance has remained relatively unrecognized. In two hundred articles reviewed, increasing dysmenorrhea was emphasized in twelve, mentioned passingly as one of the possible symptoms in seventeen and omitted altogether in the remainder. Before we appreciated this symptom only 20 per cent of our cases were diagnosed before operation, at present



FIGURE 1 Photograph of Ovary (x 1)

An early chocolate cyst, 4 mm in diameter illustrates the importance of visual exploration of the pelvis. Cysts less than 1 mm in diameter can be identified — if one looks instead of feels.



FIGURE 2 Photograph of Piece of Excised Pelvic Peritoneum (x 1/4)

This shows, below, a small "blueberry spot" and, above, red roughness.

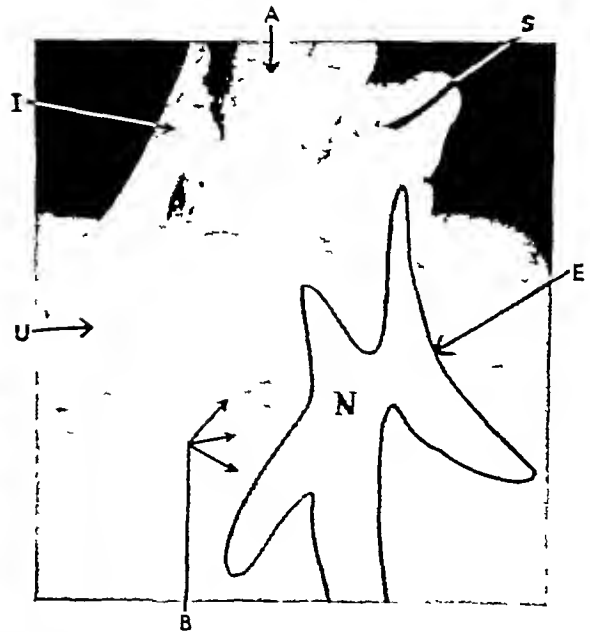


FIGURE 3 Photograph of Both Inflammatory and Endometriotic Adhesions between an Appendix Epiploicum and the Uterus (x 2)

U is the uterus, A an appendix epiploicum, and S a retracting suture. This illustrates certain differences in appearance and in nature between endometriosis and chronic pelvic inflammation. The inflammatory lesion (I) is thin sheet-like stretching. The adhesion of endometriosis (E) is strong solid contracting, note the typical stellate lines of puckering. "Blueberry spots" appear at B, and the endometriotic nodule at N.

per cent are so diagnosed, and the missed 30 per cent consists principally of patients with painless ovarian endometriomas or with early endometriosis discovered at operation for other disease or of patients who, for one reason or another, were admitted directly to the hospital without passing through the clinic. There are lessons in this last group they were admitted by a member of the house staff, the interview with a member of the clinic was—in war days—brief, and the endometriosis was recognized for the first time at operation.

A change in the time or amount of menstrual flow is also a symptom of endometriosis. Often—and from our experience, we believe, erroneously—it is called the chief symptom. In this series it was present in a third and absent in two thirds of the cases. It is therefore of no diagnostic value. The symptom may help, however, by bringing to the physician patients who recognize irregularity as pathologic but who accept periodic pain as woman's normal lot. In every case of menorrhagia, therefore, inquiry should be made regarding dysmenorrhea.

Jarring of the pelvis, from walking on a hard sidewalk, riding on a rough road, coitus, defecation or even sitting down suddenly, may increase the pain of endometriosis. The absence of this symptom means nothing. Its presence, which connotes some serious pelvic peritoneal irritation, always suggests but is not diagnostic of endometriosis. Like menorrhagia, however, this variation may cause women who accept so-called "normal dysmenorrhea" in silence to consult a physician.

Pathognomonic Sign

Pain on movement of the cervix at vaginal examination has the same pathologic significance as the pain on jarring referred to above—that is, it signifies a serious variety of peritoneal irritation, it is also frequently present but is not pathognomonic. The pathognomonic sign is the hard, fixed, invading nodule of endometriosis. The characteristic feel of this structure is a matter of tactile memory and not to be learned from print, although if one's tactile imagination is active, Figure 3 will suggest how it ought to feel. It is nearest like the feel of cancer metastases, and to the extent that it cannot always be differentiated from these it is not pathognomonic, usually, however, it can be differentiated, and then it is definitive. Certain stratagems are useful in the search for the nodules. Rectal palpation is often more rewarding than vaginal, and combined, simultaneous rectal and vaginal examination is more satisfactory than either alone. The posterior-vault peritoneum and the uterosacral ligaments, on whose anterior reaches many of the nodules occur, can be tensed for better palpation by pushing the cervix forward by the finger or pulling it downward by a tenaculum. Examination midway between periods, followed by re-examination at the

beginning of the next period, may show the nodule to be tenderer on the second occasion.

Unfortunately, nodules large enough to be palpable often indicate advanced disease, and nodules may be present but out of reach. Actually, pelvic examination substantially contributed to diagnosis in a little less than half of our cases in which the diagnosis was made. Despite a pelvis normal to palpation, therefore, the diagnosis should be made from the history alone.

Specialized Susceptibility

The occurrence of endometriosis is largely limited to one group of people. The diagnosis should not be rejected because a patient is outside this group, but the possibility should be considered in every patient within it. This group consists of women who are not having children—the sexually dormant, whether married or single.

It is often said that endometriosis causes sterility. It is true that women with advanced endometriosis are and those with early endometriosis may be sterile. Yet at least 26 cases of coexistent pregnancy and endometriosis have been collected,⁵ and this series adds a probable 10 in 2 cases old endometriosis was shown at operation soon after miscarriage, 1 patient had a ruptured tubal pregnancy and old endometriosis and 7 patients had become pregnant since the estimated onset of the disease. Parenthetically, in these 7 the pregnancies seemed temporarily to have arrested the endometriosis.

That endometriosis causes sterility is true but is not the point. The significant fact is that endometriosis occurs in women of child-bearing age who are not having children. The phrase "child-bearing age" should be clarified. The youngest patient of whom we have found record was a thirteen-year-old girl in this series. There were also 1 girl of sixteen and 7 of seventeen, eighteen or nineteen years of age.⁶ At the other extreme were 3 women of forty-seven to fifty and 1 of fifty-three years of age. All were menstruating, and all, except 2, had been menstruating for at least five years. Shortly after the menopause, endometriosis becomes a relic—3 patients, ranging in age from fifty-three to sixty-six years, had inactive residua of the disease. To analyze the phrase "are not having children" in this series over two thirds of the 200 women had never had a child. This, of course, is significant. Women with children, however, can have endometriosis,—59 of the 200 patients did,—as can the mother of a large family—13 of these mothers had five children or more. The phrase therefore signifies only women who have not had a baby recently—that is, for about five years. In this series there were 14 women who had been pregnant within the five years before discovery of the disease. But 4 of them had artificial endometriosis, caused by operation. In 2 of the 10 patients with spontaneous disease the endometriosis appeared to have started within five years

of delivery. But in each of the other 8 the symptoms of endometriosis, we believed, could be traced back to a fallow period of five years preceding the last pregnancy. In other words, of a total of 190 patients with spontaneous endometriosis — the 10 with artificial disease being subtracted from the total of 200 — the disease seemed to have begun within five years of confinement in only 2 cases.

There is contributory evidence in the thirteen mothers who had five or more children. These women all married young, had their babies early, stopped having babies and, after five years or more, developed endometriosis. Finally, although endometriosis occurs in youth, reports of its appearance before approximately five years of menstrual life are extremely rare.⁶

The most practical item in diagnosis after increasing dysmenorrhea is therefore considered to be a history of about five years of nonpregnancy preceding the disease. And it seems to make no difference whether the nonpregnancy is from inability, indecision or lack of opportunity. Palpable endometriomas confirm the diagnosis but are absent as often as present.

TREATMENT

Endometriosis is a disease for which a true specific treatment is available. Following ovarian deactivation endometriosis gradually regresses, with insignificant residua. But the price — castration — is high. In the hope of avoiding castration in advanced cases, we have begun to study temporary ovarian deactivation by small doses of radium after confirmation of diagnosis by peritoneoscopic biopsy. Masculinizing, follicular and luteinizing hormones have also been suggested, but the last two are probably as likely to harm as to help.

For such a chemical problem the future may offer a chemical solution that will restrict the surgeon to the taking of biopsies. But today he has a procedure that is reasonably efficient and less costly than castration. This consists in diagnosis while all lesions are young enough to be removed individually without castration and in prophylaxis.

The arbitrary five fallow years discussed above may be new, but there is nothing original about the concept of endometriosis as a disease of the sexually dormant.^{7, 8} Meigs⁹ calls it a physiologic response to an abnormally uninterrupted menstrual career. If the theory is sound the prophylactic is obvious — more obstetrics would engender less gynecology. Marriage at the age of seventeen and a child every three years would probably abolish endometriosis. It should be remembered that the disease itself, not eugenics, ethics or even common sense, is under consideration. Marriage at twenty and no five years without a baby would perhaps be more sensible.

An excellent opportunity for prophylaxis is offered the practitioner when he refers to the surgeon a woman with appendicitis. Because of the fre-

quency of endometriosis and of other unsuspected pelvic lesions, we believe that it is often fitting for the practitioner to suggest exploration of the pelvis in addition to removal of the appendix. Digital examination can miss an early lesion. But to the eye endometriosis is as unmistakable as chicken pox, so that no pelvis can be said to have been adequately investigated until it has been explored by vision. This necessitates a median incision which, when routinely used for appendectomy in women, has revealed a surprising amount of endometriosis.

In patients with severe dysmenorrhea, even if the symptom is not increasing, exploration is often indicated when lesser treatment fails. If no endometriosis is found, presacral sympathectomy may justify the operation. Endometriosis, which is frequent and painful, causes sterility; it is therefore sound prophylaxis to be radical about deciding to explore in suspicious cases.

Some experienced operators do not bother to excise small lesions, others allow even large lesions to remain but resect three quarters or more of the ovarian tissue in the hope of diminishing ovarian function. To us, both these procedures seem overconservative, for the following reasons: large endometriomas grow from small ones, patients with small lesions may have a great deal of pain, which ceases after removal of the lesions, subtotal oophorectomy, like subtotal thyroidectomy, is a physiologic compromise, and, finally, in severe cases, we have observed endometriomas that continued to grow after previous operation or the disease itself had destroyed all but a shell of ovarian tissue.

True conservatism, we believe, consists in spending an hour picking nodules out of a pelvis, even though castration could be done in ten minutes. We have set ourselves the alternative of complete extirpation or castration, and have taken pains and accepted risks to excise the disease whenever excision was possible. One of the 2 deaths in this series occurred from operation for endometriosis, the other from hepatic carcinoma metastatic from the colon in a patient whose incidental endometriosis had not been treated. The few exceptions to the rule were in young girls with extensive lesions in whom the treatment consisted in removal of the disease that it was mechanically practicable to remove, combined with temporary castration by small doses of radium. Obviously, the risk of radiating ova that subsequently might become impregnated should be taken only in extreme circumstances.

About half the patients in this series were castrated. To our great disappointment and despite definite improvement in diagnosis and steadily increasing willingness to resect more difficult lesions the proportion of patients castrated is not significantly lessening. Of the first 100 patients in the series, 52, and of the last 100, 45 were castrated.

patients in the series are being followed, but the results of treatment for endometriosis should not be quoted before the menopause. Among the treated patients, recurrence from the use of stilbestrol has been encountered and has so far yielded to withdrawal of the medication. It can be said that radical excision without castration may afford some relief and sometimes results in pregnancy — Payne¹⁰ reported 10 and Haydon⁸ 19 patients who became pregnant following operation, Counseller¹¹ reported ten pregnancies in 7 patients, and 3 of our patients have had one child each.

Recurrence is suspected in 2 of our patients, who are nevertheless being only watched. The 3 patients with recognized recurrences became asymptomatic following irradiation. As Pemberton¹² has pointed out, irradiation is not to be undertaken casually. The dense adhesions of the disease may bind the intestine into a dangerously immobile target for the x-rays.

SUMMARY

Endometriosis is a progressive, painful, sterilizing, crippling disease that can be both prevented and cured. Opportunities for prevention and cure are lost because no accurate clinical picture has become generally accepted and because the frequency of the disease is not appreciated.

In the female patients seen in this clinic the incidence of endometriosis was greater than that of acute appendicitis.

Endometriosis is an antivenereal disease — that is, it is associated with sexual unfulfillment. The prophylaxis seems to be early marriage and a child every few years.

Endometriosis is a new growth of menstruating endometrium that, invading and sometimes metastasizing, tends to spread through the pelvis,

causing chemical peritonitis, dense adhesions, sterility, destruction of ovaries and stricture of the pelvic intestine. Ovarian hormone is necessary to the progress of the disease. The course, which is reversed by ovarian deactivation, may be arrested by excision of the lesions. To arrest without castration necessitates diagnosis before the lesions have become mechanically unresectable.

Contrary to general opinion, clinical diagnosis is usually possible. It depends on ability to separate from a mass of adventitious pelvic symptoms and signs the following basic syndrome of endometriosis: cumulatively increasing pain at the time of the period occurring after about five years of menstruation without pregnancy. Endometriotic nodules are pathognomonic but often not large enough to be felt, in which event the diagnosis should be made on the basis of the history alone.

Because endometriosis can be seen long before it can be felt the practitioner should be as radical about advising surgical exploration as the surgeon is conservative about castration.

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BRIGHT'S DISEASE CLINICAL MANIFESTATIONS IN RELATION TO ETIOLOGY AND PROGNOSIS*

RAYMOND D. PRUITT, M.D.

ROCHESTER, MINNESOTA

IN 1827 Bright¹ pointed out the association between dropsy, albuminuria and hardened kidneys. In this simple correlation he established the foundation for a multitude of observations that accumulated in succeeding years under the caption of "Bright's disease." It soon became apparent that, from both a clinical and a pathological standpoint, Bright's disease was not an entity but an assemblage of diseases. Subsequent efforts to achieve specificity resulted in many classifications, some accurate and many detailed. But what is satisfying to an expert in the field is not always expedient for one whose circumstances demand familiarity with the range of clinical medicine. As a result, physicians have frequently resorted to the broad and time-honored diagnosis of Bright's disease rather than attempting to drag out a rarely recognized term buried deep in some current classification of vasculorenal disease.

But Bright's disease is not a satisfying diagnosis. Between excess of generalization and impracticable specificity there should be some compromise. A simple classification of vasculorenal disease from the point of view of a clinician should be one in which the nomenclature is descriptive of clinical findings. It need not become involved with pathological terms such as "small granular kidneys," "large pale kidneys," "primarily and secondarily contracted kidneys" and "flea-bitten kidneys."

FUNDAMENTAL CLINICAL MANIFESTATIONS

The important clinical findings in Bright's disease ("vasculorenal disease") is an equally comprehensive and more descriptive term) are renal insufficiency, dropsy and hypertension. If, in a scheme of diagnosis, importance is to be attached to these clinical manifestations, it is essential that the character of each be understood. For this reason the following elaboration of the nature of each is undertaken.

Renal Insufficiency

It is apparent that one of the most significant effects of disease on the kidney is impairment of functional capacity. The degrees of damage may be described under three headings: latent renal damage, compensated renal insufficiency and uncompensated renal insufficiency.

Latent renal damage. The existence of latent impairment of kidney function is dependent on the

large reserve capacity of the normal organ. Under this heading are included cases in which there is no demonstrable reduction in the functional capacity of the kidney. Responses to all tests are within the normal range. Yet a pathologic process known to affect the kidney exists. An example of this type of renal damage is found in early essential hypertension.

Compensated renal insufficiency. At this stage of renal damage, a sufficient proportion of the functioning elements of the kidney have been damaged or destroyed to eliminate a large measure of the reserve capacity of the organ. So long as the patient is in good general health, the concentration of urea in the blood remains normal. There is a reduction, however, in the capacity of the kidney to do a specific amount of work in a limited time, as demonstrated by the urea-clearance test. The power to produce concentrated or a dilute urine is impaired. With the development of an unusual strain on the organ actual renal insufficiency develops and the concentration of blood urea may rise.

Uncompensated renal insufficiency. With the development of this degree of destruction of kidney substance, not only are the reserves of the organ exhausted but also the capacity to care for the current excretory load is lost. The concentration of urea in the blood is elevated and, unless compensation is restored, mounts steadily. The end result of this sequence is the development of the uremic state. The term "uremia" or "uremic state" may well be reserved to describe that terminal phase of renal insufficiency during which certain overt manifestations of kidney failure develop—namely, somnolence, confusion, nausea, vomiting, muscular irritability and convulsive seizures.

Dropsy

In the absence of cardiac failure, dropsy in a case of chronic renal disease is the outward and visible sign of a derangement in the metabolic processes of the body that has been designated the "nephrotic state." The initial factor in the development of this syndrome is probably the loss of excessive amounts of albumin in the urine. The albuminuria itself is believed to be secondary to increased permeability of the glomerular membranes, permitting the smaller molecules of the normally retained serum proteins to pass into the urine. Secondary to the

*From the Division of Medicine, Mayo Clinic.

loss of serum proteins there develops hypoproteinemia associated with a disturbance in the osmotic equilibria of the blood and tissue fluids, culminating in the accumulation of increased amounts of fluid in the tissue spaces. The hyperlipemia that is also a feature of the nephrotic syndrome is probably a compensatory reaction directed toward restoration of a more nearly normal osmotic relation.

Hypertension

Of the three major clinical manifestations of vasculorenal disease, elevation of the blood pressure is the most frequent. Foregoing for the moment any distinction between angiospastic processes and the more usual sclerosis and narrowing of the arterioles, one may divide the hypertensive reaction of vasculorenal disease into four groups, according to the classification of Keith, Wagener and Barker,² in which certain changes in the ocular fundi are of fundamental importance. The divisions are as follows:

Group 1 Patients who have only mild narrowing or sclerosis of the retinal arterioles fall into this division.

Group 2 Patients are placed in this category if they have moderate to marked sclerosis of the retinal arterioles, whether of the chronic type—characterized especially by exaggeration of the arterial reflex and arteriovenous compression—or of the postangiospastic type—characterized especially by, generalized and localized irregular narrowing of the arterioles.

Group 3 Patients who have retinitis of the angiospastic type—characterized especially by edema, cotton-wool patches and hemorrhages in the retina, superimposed on a combination of sclerotic and spastic lesions in the arterioles—belong to this group.

Group 4. This group comprises patients with measurable edema of the disks in addition to the findings described above.

Although the arteriolar changes are readily studied clinically only in the retina, pathological investigations support the postulate that the arteriolar disease in hypertension is generalized.³⁻⁵ Therefore, in cases of hypertension, an accurate descriptive diagnosis is "diffuse arteriolar disease with hypertension, Group 1, 2, 3 or 4."

ETIOLOGY

Regardless of the nature of the specific disease affecting the vasculorenal system, the major clinical manifestations may be described with reasonable consistency in terms of the triad discussed above. To this proposition there is a corollary: Bright's disease is not an entity but an assemblage of diseases grouped together, not because of similarity of cause

but because of similarity of effect. In the following paragraphs the relation between certain specific causes and the triad of effects is elaborated, Bright's disease being analyzed from the etiologic standpoint whereas the fundamental unity found in the clinical expressions is retained.

Chronic Glomerulonephritis

The term "chronic glomerulonephritis" implies the existence of an earlier phase of the disease that in some cases was acute, almost explosive. The patient so afflicted was obviously ill, with an elevated temperature and labored respirations. The urine contained many casts and erythrocytes and much albumin. Anasarca, hypertension and renal insufficiency may have been present simultaneously in this acute phase.

In contrast, this preliminary stage may have had an insidious onset unattended by symptoms. Its existence could be defined only by examination of the urine, in which there were small amounts of albumin and sometimes a few casts, erythrocytes and pus cells.

Slowly or rapidly, but fortunately not inevitably, chronic glomerulonephritis evolves from the nephritis of acute or insidious onset. The initial lesion was in the glomerulus. As the destructive changes progress in this portion of the nephron, any one or any combination of the three clinical features of vasculorenal disease may develop concurrently or sequentially. Furthermore, although two or all three manifestations may be present, one component may be mild and another severe. Finally, a patient may pass through phases during which, in succession, he suffers primarily from one aspect of the triad, he recovers from this and he succumbs to another expression of the disease.

It is not expedient or essential to clarify to present illustrations of all these potential combinations. Two examples are sufficient. First, a patient with chronic glomerulonephritis and findings pathognomonic of all phases of the triad may present the following: a blood urea concentration of 200 mg per 100 cc (normal 15 to 40 mg), large amounts of albumin in the urine, a value for serum protein of 3.5 gm per 100 cc (normal 6 to 8 gm), with an albumin-globulin ratio of 1.0:1.2 (normal 2.0:1.0), anasarca, and hypertension with associated arteriolar disease. A descriptive diagnosis in such a case is chronic glomerulonephritis with severe renal insufficiency (as indicated by the elevated blood urea level), nephrotic syndrome (as demonstrated by albuminuria, hypoproteinemia, reversal of the normal albumin-globulin ratio and anasarca) and superimposed diffuse arteriolar disease with hypertension.

In contrast is the patient with a relatively pure nephrotic syndrome. Typical findings in such a case are a blood urea value of 32 mg per 100 cc,

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age in whom the illness has been present for a similar period. Each has renal insufficiency with a blood urea concentration of 150 mg per 100 cc. But one has superimposed diffuse arteriolar disease with hypertension, Group 3, whereas the other has an essentially normal arteriolar system. The prognosis for the latter is much better than that for the former.

Equally significant is the consideration of 2 patients each with a moderately severe nephrotic syndrome. One has normal renal function so far as can be determined by tests, and the other has uncompensated renal insufficiency. All else being equal, the prognosis for the latter is less favorable than that for the former, not only because two pathologic processes are worse than one but also because treatment of one manifestation often entails application of measures unfavorable to the other. The patient with renal insufficiency has lost his ability to produce a concentrated urine. Therefore he must excrete large amounts of urine to avert a rise in the blood urea concentration. But the wisdom and the feasibility of administering large amounts of fluid to the patient with an advanced nephrotic

syndrome constitute problems that evade simple resolution.

* * *

More extended consideration of therapeutic problems in cases of Bright's disease is not appropriate to this limited discussion. If there is value in undertaking the treatment of vasculorenal disease by application of measures directed toward alleviation of renal insufficiency, the nephrotic syndrome or hypertension, that value is apparent in the illustrations elaborated above.

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marked albuminuria, a concentration of serum protein of 3.5 gm per 100 cc, with an albumin-globulin ratio of 1:0.12, and generalized anasarca, but with normal blood pressure and no definable narrowing or sclerosis of the retinal arterioles. Such a patient presents evidence indicative of adequate renal function and of a normal arteriolar system without hypertension in the presence of a well developed nephrotic syndrome.

As a concluding observation regarding chronic glomerulonephritis it may be noted that renal insufficiency unattended by hypertension or by the nephrotic syndrome is probably the rarest clinical manifestation of the disease. Such cases occur, however, and a patient may pass into the uremic state and die without the development of either of the other two features of the triad.⁶

Essential Hypertension

Primary consideration was given above to chronic glomerulonephritis because of its basic relation to the three cardinal manifestations of vasculorenal disease. During the course of chronic glomerulonephritis, hypertension may or may not appear and may or may not be a symptom of the disease. But hypertension may also occur as an isolated phenomenon, apparently unrelated either to chronic glomerulonephritis or to any of the other entities affecting the vasculorenal system. In this event, the clinical manifestation becomes the disease and bears a name, albeit an unrevealing one — "essential hypertension." From the standpoint of incidence alone, essential hypertension is the most important entity included under the term "Bright's disease."

Whereas the site of the initial lesion in chronic glomerulonephritis can be identified with precision, the primary change in essential hypertension remains indeterminate. The kidney undoubtedly becomes involved in advanced stages of the disease, but that the primary lesion is renal is far from an established fact. Rather, the initial lesions in essential hypertension appear to be arteriolar and so generalized as to justify the caption "diffuse arteriolar disease."

However different their origins, chronic glomerulonephritis and essential hypertension in their final stages may be confusingly similar. Although the nephrotic syndrome is peculiar to glomerulonephritis, renal insufficiency and hypertension are frequently associated in the terminal stages of both diseases. Whereas marked albuminuria with many casts and erythrocytes is usually indicative of primary glomerulonephritis, all these urinary findings may be duplicated in the terminal stages of severe hypertension. Sometimes the history or the age of the patient supplies evidence helpful in defining the initial lesion. A previous episode of acute glomerulonephritis, a record of albuminuria for years prior to the onset of hypertension and youth of the

patient may suggest that the initial lesion was in the glomeruli. On the other hand, a history of high blood pressure of many years' duration, without other indications of impaired health, is more suggestive of primary hypertensive disease. In some cases it remains for the pathologist to establish whether the primary lesion was arteriolar or glomerular, but the decision is not always achieved with finality even at this ultimate stage.

Other Conditions

A sound knowledge of chronic glomerulonephritis and essential hypertension and their interrelations is fundamental to an understanding of the rarer and often simpler causes of Bright's disease. One of these is chronic pyelonephritis, in which extensive destruction of renal tissue by an infectious process may lead eventually to advanced renal insufficiency with superimposed diffuse arteriolar disease and hypertension. In polycystic disease, destruction of the renal parenchyma is accomplished by a different means but with similar results. Toxic processes may lead to tubular damage and suppression of formation of urine, with consequent acute renal insufficiency usually unassociated with appreciable hypertension or the nephrotic state. Lymphoblastomatous or amyloid infiltrations of the kidney may give rise to a relatively pure nephrotic syndrome later complicated by renal insufficiency. Periarteritis nodosa is sometimes attended by hypertension and ultimately by renal insufficiency. But whatever the pathogenesis of the lesion in the vasculorenal system, the overt expressions of the disease can be related in most cases to one or more of the well established patterns.

PROGNOSIS

In concluding this survey it is reasonable to turn from the consideration of diagnosis and classification to the problems of prognosis and treatment, in which the delineation of the triad of renal insufficiency, nephrotic syndrome and hypertension is also of value. Prognosis is not a precise science and demands calculations more subtle than those of arithmetic. Some insight into the future of the patient with vasculorenal disease can be achieved, however, if it is recognized that the course is dependent on the number of the clinical manifestations that are combined, as well as on the severity of the individual components. This generalization is applicable to the more frequent etiologic processes in vasculorenal disease — namely, chronic glomerulonephritis, essential hypertension and chronic pyelonephritis. The significance of the generalization is minimized in cases in which the primary process is one of the rarer entities, such as lymphoblastoma, amyloid disease or periarteritis nodosa.

In illustration, comparison may be made of chronic glomerulonephritis in 2 patients of similar

abscess is the upper and posterior portion of the right lobe.⁴ Abscesses in this lobe often extend upward and may penetrate the diaphragm and rupture into the lung. It is well known that amebic abscesses occur in many other organs.

Hepatic disease complicating amebiasis usually appears one to three months after an attack of dysentery, but it may manifest itself during an attack or much later. The symptoms of hepatic abscess include pain or discomfort over the liver, with occasional reference to the right shoulder, irregular and intermittent fever, sweats, chills, nausea, vomiting, weakness and loss of weight. Jaundice, except in mild degree, is unusual. Diarrhea or dysentery is present in only about a fourth of the cases of proved liver disease. The diagnosis of hepatic amebiasis depends primarily on a high index of suspicion. Not infrequently a diagnosis of fever of undetermined origin is carried for weeks, because the clinical picture is not specific and the physician does not consider amebiasis as a possible cause of the symptoms. Liver-function studies are not diagnostic, they are merely suggestive and help to point the finger of suspicion at the liver. Leukocytosis of moderate degree is usually present. Stool examination for amebic cysts is, of course, of paramount importance, but is often negative even in the most competent hands. The use of intravenous Diodrast and planography is advocated in attempting to locate a liver abscess. Because of its specificity in amebiasis, emetine constitutes a therapeutic test of great value, but since the drug is a potent protoplasmic poison, it should be used circumspectly.

The following case reports are presented to illustrate the hepatic complications of amebiasis, as well as the extreme difficulty of diagnosis. Because of the obscure nature of the disease it is easy to see how errors in treatment can occur unless one is constantly aware of the possible existence of amebiasis.

CASE 1 R C D, a 35-year-old man, was admitted to the hospital, on October 18, 1945, for the treatment of malaria. The significant fact in the history was service in the Southwest Pacific area, during which he had had malaria and amebic dysentery. Prior to this admission he had suffered from diarrhea and pain in the left upper quadrant of the abdomen, accompanied by chills, fever and sweats.

Physical examination on admission revealed the patient to be acutely ill. The only significant finding was marked tenderness and muscle spasm in the left upper quadrant of the abdomen with no definite splenomegaly. The temperature was 102°F., the pulse 100, and the respirations 22. Examination of the blood showed a red-cell count of $\pm 4,010,000$, with a hemoglobin of 86 per cent (Sahli), and a white-cell count of 13,000, with 81 per cent neutrophils. No malarial parasites were found in the blood smear.

The patient was placed on a regimen of quinacrine, which had no effect on the clinical course—the patient suffered from fever, chills and sweats at irregular periods, with weakness and occasional nausea and vomiting. The tenderness and pain in the left upper quadrant persisted. The red-cell count gradually diminished, and a transfusion of 500 cc of whole blood was given on three occasions. Examination of the stools revealed no amebic cysts or motile forms. Sigmoideoscopic examination was negative. The cephalin-flocculation test was +, and the icterus index was 9 and 3

on two occasions. A gastrointestinal x-ray series was negative. A sense of fullness developed in the epigastrium, together with slight enlargement of the liver. At the same time the patient's sense of well being gradually improved, and the pain in the left upper quadrant of the abdomen slowly subsided. No splenomegaly could definitely be made out at any time.

On November 21 a definite tender mass about the size of a lemon was noted in the left upper abdominal quadrant. Surgical exploration disclosed an encapsulated abscess in the region of the anterior surface of the left lobe of the liver. The abscess was incised freeing "anchovy-paste" pus, drained by suction, packed and irrigated daily with 1:1000 solution of emetine hydrochloride. At the same time 20 mg of emetine hydrochloride was administered intramuscularly three times a day for 7 days.

On November 25, while the patient's condition was slowly improving, he developed a chill, followed by a rise in temperature to 103.4°F. A blood smear revealed the presence of *Plasmodium vivax*. Response to quinacrine hydrochloride was prompt, and convalescence continued uneventfully. The patient made a complete recovery.

In the early stages of the illness the patient's chief complaint was directed entirely toward the left upper quadrant. The consistently negative blood smears and the failure to respond to quinacrine on admission removed malaria from the list of diagnostic possibilities, although this disease had appeared to be the likeliest cause of the chills and fever. Subsequently, intensive studies made to rule out the presence of blood-stream infection and renal suppuration were negative. The possibility of amebiasis had been entertained, but no definite findings were noted. In retrospect, we believe that the use of emetine early in the course of hospitalization would have been of significant diagnostic value, and might conceivably have prevented the formation of a full-blown liver abscess. Despite the failure to find the pathogen in the feces, the pus or the wall of the abscess, it was considered certain, on clinical grounds, that the patient did have an amebic abscess. The pus was characteristically free of pathogens, although they are often found in the wall of the abscess.

CASE 2 W F B, a 27-year-old farmer, had been discharged from the Army on January 20, 1946, shortly after his return from the Southwest Pacific. At the time of discharge he was in good health. He had never been ill during his service in the Army and did not recall any minor episodes of diarrhea or fever. About 3 weeks prior to admission to the hospital he became ill, with fever and pain in the right chest. He consulted his family physician, who treated him for malaria without improvement and who, about 10 days before admission, thought that there was fluid in the right chest. No x-ray film was taken, nor was a thoracentesis performed. On admission the patient complained of mild pain in the lower right chest on deep inspiration, as well as a slight cough without expectoration. There had been no dyspnea. He had lost 15 pounds in the preceding 2 weeks. He had had frequent head colds for several years. Several chest x-ray films taken in the Army had been negative for tuberculosis. He had had no significant illness or operations.

Examination revealed a well developed and well nourished man, who was ambulant and not acutely ill. Significant findings were slight impairment of percussion resonance over the extreme right base of the chest posteriorly, distant breath sounds in the same area and occasional superficial fine rales. No friction rub could be heard. The liver edge, which was palpable on deep inspiration just under the right costal margin, was somewhat tender. Heavy fist percussion over the liver elicited pain. The temperature was 100°F., the pulse 88, and the respirations 18.

HEPATIC COMPLICATIONS OF AMEBIASIS*

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THE purpose of this paper is to invite attention to some of the bizarre and puzzling manifestations of amebiasis that have been encountered, with special reference to hepatic complications. Pitfalls in diagnosis may be easily avoided if the possibility of amebiasis is kept in mind. It should be remembered that dysentery is an infrequent manifestation of amebiasis. Even lesions in the large intestine are not invariably found on sigmoidoscopic examination. Therefore, despite the absence of a history of dysentery, amebiasis must be considered in the differential diagnosis of many bizarre clinical syndromes.

The disease is not restricted by geography or climate. Poor sanitation and poor hygiene are chiefly responsible for its spread. It is frequent in the southern states but is not rare in the northern ones. In 1933 the disease intruded itself into the national consciousness as a result of the outbreak of amebic dysentery at the Century of Progress Exposition in Chicago. At present, a far more serious source of dissemination has appeared in our work at this large hospital we are seeing ever-increasing numbers of returning service men affected with tropical diseases. Bomford,¹ in an article on chronic amebiasis in soldiers of the British Army, emphasizes the fact that awareness of this disease and its many manifestations results not only in early diagnosis but also in a reduction of the hazards of dissemination. In 1942 Faust² estimated the incidence of carriers to be 20 per cent of the total population. What effect the recent influx of a host of carriers will have on this already menacing number time alone will tell. In the Veterans Administration hospitals physicians are in a particularly favorable position to observe this disease and to check its spread by prompt diagnosis and adequate treatment. The large number of veterans of World War II who will pass through these hospitals within the succeeding months and years constitutes a challenge to the efficiency of the medical profession. The future will clearly show how effective the fight against amebiasis has been. A high index of suspicion is the keynote of early diagnosis.

The morphology of the parasite is well known, but differentiation of this pathogenic ameba from normal nonpathogenic inhabitants of the human

intestinal tract is difficult. The motile vegetative forms or trophozoites, which are invasive and are responsible for the pathologic changes characteristic of the disease, do not serve as a means of transmission. They are short lived outside the body and probably cannot survive passage through the stomach following ingestion of contaminated food. The cysts are the infecting agents, because they are resistant to marked changes in their environment. It is essential to realize that ordinary chlorination does not destroy the encysted forms, which at freezing temperatures can remain viable for weeks. The character of the stools determines the form of the parasites present. In the presence of diarrhea, it is exceptional to find anything but trophozoites. If the formed stools are passed, only cysts are usually found. Needless to say, careful stool examinations by experienced technicians are helpful in the diagnosis. It is reiterated, however, that the absence of the pathogen from the stools is not positive evidence that amebic infection is not present. Sigmoidoscopy should always be performed because the diagnosis of amebic colitis is frequently made from the gross appearance of the colonic ulcers, and in addition, the organism is often found in smears taken from the floor of these ulcers. It is not the purpose of this paper to outline diagnostic procedures, which are covered in standard texts.

Invasion of the submucosa of the wall of the colon may be followed by the entry of *Endamoeba histolytica* into radicles of the portal vein and metastasis of the infection to the liver. This is followed by amebic hepatitis or amebic abscess. Such abscesses may be single or multiple, acute or chronic. In an analysis of 1000 cases of amebic dysentery Payne³ found hepatitis to be present in over 50 per cent and liver abscess in almost 3 per cent, the latter figure is in close agreement with that of other investigators. — Craig⁴ observed liver abscesses in 5 per cent of 745 cases. The term "amebic hepatitis" is used to indicate the early phase of amebic hepatic disease before frank abscess can be diagnosed. Ochsner and DeBakey⁵ emphasize the differentiation of the two. Sodeman and Lewis⁶ stress the fact that it is impossible to be certain clinically that small single or multiple abscesses are not present during the early phase, when diagnosis and treatment are extremely important.

Multiple foci of necrosis may coalesce to form a single large abscess. Leukocytic infiltration of the wall occurs even in the absence of secondary bacterial infection. The most frequent seat of the

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abscess is the upper and posterior portion of the right lobe.⁴ Abscesses in this lobe often extend upward and may penetrate the diaphragm and rupture into the lung. It is well known that amebic abscesses occur in many other organs.

Hepatic disease complicating amebiasis usually appears one to three months after an attack of dysentery, but it may manifest itself during an attack or much later. The symptoms of hepatic abscess include pain or discomfort over the liver, with occasional reference to the right shoulder, irregular and intermittent fever, sweats, chills, nausea, vomiting, weakness and loss of weight. Jaundice, except in mild degree, is unusual. Diarrhea or dysentery is present in only about a fourth of the cases of proved liver disease. The diagnosis of hepatic amebiasis depends primarily on a high index of suspicion. Not infrequently a diagnosis of fever of undetermined origin is carried for weeks, because the clinical picture is not specific and the physician does not consider amebiasis as a possible cause of the symptoms. Liver-function studies are not diagnostic, they are merely suggestive and help to point the finger of suspicion at the liver. Leukocytosis of moderate degree is usually present. Stool examination for amebic cysts is, of course, of paramount importance, but is often negative even in the most competent hands. The use of intravenous Diodrast and planography is advocated in attempting to locate a liver abscess. Because of its specificity in amebiasis, emetine constitutes a therapeutic test of great value, but since the drug is a potent protoplasmic poison, it should be used circumspectly.

The following case reports are presented to illustrate the hepatic complications of amebiasis, as well as the extreme difficulty of diagnosis. Because of the obscure nature of the disease it is easy to see how errors in treatment can occur unless one is constantly aware of the possible existence of amebiasis.

CASE 1 R.C.D., a 35-year-old man, was admitted to the hospital, on October 18, 1945, for the treatment of malaria. The significant fact in the history was service in the Southwest Pacific area, during which he had had malaria and amebic dysentery. Prior to this admission he had suffered from diarrhea and pain in the left upper quadrant of the abdomen, accompanied by chills, fever and sweats.

Physical examination on admission revealed the patient to be acutely ill. The only significant finding was marked tenderness and muscle spasm in the left upper quadrant of the abdomen with no definite splenomegaly. The temperature was 102°F., the pulse 100, and the respirations 22. Examination of the blood showed a red-cell count of 4,010,000, with a hemoglobin of 86 per cent (Sahli), and a white-cell count of 13,000, with 81 per cent neutrophils. No malarial parasites were found in the blood smear.

The patient was placed on a regimen of quinacrine, which had no effect on the clinical course — the patient suffered from fever, chills and sweats at irregular periods, with weakness and occasional nausea and vomiting. The tenderness and pain in the left upper quadrant persisted. The red-cell count gradually diminished, and a transfusion of 500 cc of whole blood was given on three occasions. Examination of the stools revealed no amebic cysts or motile forms. Sigmo-
scopic examination was negative. The cephalin-flocculation test was +, and the icterus index was 9 and 3

on two occasions. A gastrointestinal x-ray series was negative. A sense of fullness developed in the epigastrium, together with slight enlargement of the liver. At the same time the patient's sense of well being gradually improved, and the pain in the left upper quadrant of the abdomen slowly subsided. No splenomegaly could definitely be made out at any time.

On November 21 a definite tender mass about the size of a lemon was noted in the left upper abdominal quadrant. Surgical exploration disclosed an encapsulated abscess in the region of the anterior surface of the left lobe of the liver. The abscess was incised freeing "anchovy-paste" pus, drained by suction, packed and irrigated daily with 1:1000 solution of emetine hydrochloride. At the same time 20 mg. of emetine hydrochloride was administered intramuscularly three times a day for 7 days.

On November 25 while the patient's condition was slowly improving he developed a chill, followed by a rise in temperature to 103.4°F. A blood smear revealed the presence of *Plasmodium vivax*. Response to quinacrine hydrochloride was prompt and convalescence continued uneventfully. The patient made a complete recovery.

In the early stages of the illness the patient's chief complaint was directed entirely toward the left upper quadrant. The consistently negative blood smears and the failure to respond to quinacrine on admission removed malaria from the list of diagnostic possibilities, although this disease had appeared to be the likeliest cause of the chills and fever. Subsequently, intensive studies made to rule out the presence of blood-stream infection and renal suppuration were negative. The possibility of amebiasis had been entertained, but no definite findings were noted. In retrospect, we believe that the use of emetine early in the course of hospitalization would have been of significant diagnostic value, and might conceivably have prevented the formation of a full-blown liver abscess. Despite the failure to find the pathogen in the feces, the pus or the wall of the abscess, it was considered certain, on clinical grounds, that the patient did have an amebic abscess. The pus was characteristically free of pathogens, although they are often found in the wall of the abscess.

CASE 2 W.F.B., a 27-year-old farmer, had been discharged from the Army on January 20, 1946, shortly after his return from the Southwest Pacific. At the time of discharge he was in good health. He had never been ill during his service in the Army and did not recall any minor episodes of diarrhea or fever. About 3 weeks prior to admission to the hospital he became ill, with fever and pain in the right chest. He consulted his family physician, who treated him for malaria without improvement and who, about 10 days before admission, thought that there was fluid in the right chest. No x-ray film was taken, nor was a thoracentesis performed. On admission the patient complained of mild pain in the lower right chest on deep inspiration, as well as a slight cough without expectoration. There had been no dyspnea. He had lost 15 pounds in the preceding 2 weeks. He had had frequent head colds for several years. Several chest x-ray films taken in the Army had been negative for tuberculosis. He had had no significant illness or operations.

Examination revealed a well developed and well nourished man, who was ambulant and not acutely ill. Significant findings were slight impairment of percussion resonance over the extreme right base of the chest posteriorly, distant breath sounds in the same area and occasional superficial fine rales. No friction rub could be heard. The liver edge, which was palpable on deep inspiration just under the right costal margin, was somewhat tender. Heavy fist percussion over the liver elicited pain. The temperature was 100°F., the pulse 88, and the respirations 18.

Examination of the blood disclosed a normal red-cell count and hemoglobin, with a white-cell count of 15,900 and a normal differential. No malarial parasites were found in the smear. Urinalysis showed a few white cells per high-power field. The sedimentation rate was 3 mm in 1 hour. Repeated sputum specimens were negative for tubercle bacilli. An intradermal tuberculin test was positive. Stool examinations for ova and parasites were negative. Blood agglutination tests for typhoid, paratyphoid A and B, undulant and typhus fevers were negative. A prostatic smear revealed a few pus and epithelial cells but no bacteria.

A roentgenogram of the chest taken on February 25 showed obliteration of the right costophrenic angle probably due to fluid, the lung fields were clear. Examination was repeated on March 20, when the diaphragms were smooth in contour and the costophrenic angles were clear. Another roentgenogram, taken on April 6, disclosed clear lung fields but abnormal elevation of the right dome of the diaphragm. Intravenous and retrograde pyelography revealed no abnormalities.

The patient ran an irregular, febrile course, the temperature ranging from 98 to 102°F almost daily. There was no response to penicillin and sulfadiazine. For 6 days, 65 mg of emetine hydrochloride was administered intramuscularly every day, concomitantly with oral administration of Diodoquin. Within 24 hours the temperature became normal and remained so. The patient began to regain his lost weight and soon recovered his former sense of well being. The hepatic tenderness also subsided, and the liver edge was no longer palpable. At no time was any abnormality noted on sigmoidoscopic examination.

Despite the normal sigmoidoscopic findings and the failure to demonstrate *E. histolytica* in the stools, the dramatic response to emetine and Diodoquin leaves little doubt that this patient had a liver abscess due to amebic infection. It is not unusual for hepatic abscesses to incite diaphragmatitis, pleuritis and pleural effusion, and this chain of events is considered to have occurred in this case. So far as could be determined, the hepatic abscess subsided. Further observation is warranted, however, since relapses may occur, necessitating surgical drainage.

CASE 3 U W, a 25-year-old Negro veteran of the North Burma campaign, had been discharged from the Army because of accumulated points on September 1, 1945. His health as a civilian had been good, and he had never been ill while in the service. On the day of discharge he suddenly developed severe, cramping pain in the upper abdomen, with nausea and vomiting, the stools were normal. The symptoms became progressively worse, and on September 7 he was admitted to the hospital.

On physical examination the patient was acutely ill and appeared to be in severe pain, rolling and tossing in bed. He lay with the knees flexed on the abdomen. He was perspiring freely. There was rigidity of the abdominal muscles in the upper half of the abdomen, with marked tenderness. On palpation there was a sensation of fullness in the upper abdomen. The lower abdomen was soft, no jaundice was noted. Rectal examination was negative. The temperature was 99.2°F, the pulse 100, and the respirations 20. Examination of the blood disclosed a red-cell count of 2,050,000, with a hemoglobin of 59 per cent (Sahli), and a white-cell count of 20,950, with 80 per cent neutrophils. The prothrombin time was 25 seconds (normal, 18 seconds). The total serum protein was 8.7 gm per 100 cc, with an albumin of 3.0 and a globulin of 5.7 gm. The cephalin-flocculation test was ++++. The icterus index was 5.7. A bromsulphalein test showed 10 per cent retention of the dye at 45 minutes and 5 per cent at 60 minutes. A blood smear for malaria was negative. A roentgenogram of the abdomen was negative, as was a urinalysis.

It was thought by the surgeon that an exploratory laparotomy should be done because of the possibility of a perforated duodenal ulcer. Operation disclosed an enlarged liver of firm consistence, with fine nodules on its surface. The postoperative course was uneventful except for fever and

nausea. On September 22 the patient developed diarrhea and examination of the stool showed *E. histolytica*. He was placed on emetine hydrochloride, carbarsone and later Diodoquin, with prompt subsidence of the temperature and symptoms. On October 14, during convalescence, he suddenly developed chills and fever. A blood smear was positive for *P. vivax*. The white-cell count was 5600, with 60 per cent neutrophils. Quinacrine obtained prompt and satisfactory results. The patient left the hospital on October 28, fully recovered.

The pathological report was as follows:

Histologic examination reveals a section of liver whose portal canals are infiltrated with numerous inflammatory cells, mostly round cells. Some of these are plasma cells. There is a scattering of eosinophils. Free hemorrhage is noted in the interstitial tissue. There is early connective tissue replacement, with early cirrhotic changes. No specific organism is noted in the section. There are no parasitic ova. There are some attempts at biliary regeneration. Diagnosis: hepatitis, with early cirrhotic changes.

If the possibility of amebic hepatitis had been seriously considered in this case, it is likely that surgical intervention could have been avoided. At this stage, treatment with emetine is effective and often prevents the development of large liver abscesses requiring surgical drainage. It is interesting to note that there was a well marked leukocytosis, as well as a clinical picture of an acute surgical abdomen. Even if one is aware of the possibility of acute amebic hepatitis, it is difficult to see how surgery can be withheld in some cases of this type. The therapeutic test of emetine, if time permits, is a prompt help in diagnosis. Another point of interest in this case was the absence of jaundice, despite the diffuse hepatitis.

CASE 4 V B, a 34-year-old man, was admitted to the hospital on November 22, 1945. Five weeks previously, while returning from the Southwest Pacific, he had developed abdominal cramps and diarrhea, with blood and mucus in the stools. Two days before admission these symptoms recurred. The diarrhea soon became less marked, but anorexia and pain over the liver set in. There was no nausea or vomiting. No other significant facts were uncovered in the history.

Physical examination revealed a moderately ill but well developed and well nourished man. The abdomen was soft, flat and not tender. On deep inspiration the edge of the liver was palpable and tender. No jaundice was present. The temperature was 102.6°F and the pulse 86. The blood pressure was 130/90. A clinical diagnosis of amebic dysentery and hepatitis was made.

Examination of the blood showed a hemoglobin of 96 per cent (Sahli) and a white-cell count of 18,100, with 83 per cent neutrophils, of which 15 per cent were nonsegmented forms. No malarial parasites were seen in a thick blood smear. The cephalin-flocculation test was +++, and the icterus index 5. On November 23 trophozoites of *E. histolytica* were identified in a stool specimen.

The temperature was remittent, reaching 104.4°F. 2 days after admission emetine therapy was instituted on November 23 and continued in a daily dosage of 65 mg intramuscularly for 7 days. Diodoquin was subsequently administered for 3 weeks. The temperature subsided and reached a normal level on December 1, after which it remained normal. Symptomatic improvement was quite marked by November 28.

The patient made an uneventful recovery and was discharged from the hospital on January 17, 1946. Prior to discharge laboratory studies were repeated and revealed a normal white-cell count and differential. The cephalin-flocculation test was ++, and the bromsulphalein-retention test was normal. The icterus index was 5.8. A chest x-ray film was normal. Stool studies disclosed no pathogenic organisms.

This case provides an example of prompt diagnosis and early institution of treatment. The results were gratifying in that shortly after institution of therapy the patient showed marked improvement and proceeded to an uneventful recovery. This case illustrates the concomitance of amebic dysentery and hepatitis, probably in the preabscess stage. The early diagnosis was of course aided by the presence of diarrhea and the finding of the motile vegetative form of *E. histolytica* in the stool.

SUMMARY

Amebiasis constitutes a challenge not only to the medical profession at large but also to the physicians of the Veterans Administration. Because of the bizarre symptomatology, the diagnosis of amebiasis is beset with many difficulties and pitfalls. The great number of potential carriers of *Endamoeba histolytica* makes the problem one of immediate importance. It is imperative that physicians be

acquainted with the problem of amebiasis and be constantly on the alert to make the diagnosis early. Prompt therapy is the only method of preventing the serious and sometimes fatal complications of the disease.

Four cases of amebiasis with hepatic complications are presented, with a view to emphasizing the difficulties of diagnosis. It is anticipated that such cases will become more frequent within the next few years.

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CLINICAL NOTE

FRIEDLANDER-BACILLUS MENINGITIS TREATED WITH STREPTOMYCIN*

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INTEREST in the treatment of local and general infections caused by organisms ordinarily resistant to the usual antibiotics has become increasingly stimulated by recognition of the fact that within recent years isolated cases have been reported in which successful results were obtained. In 1943 Ransmeier and Major¹ reported a case of septicemia associated with Friedländer-bacillus meningitis and published the report after an analysis of 29 cases of similar type that had been collected from the literature. In the 30 cases reported so far, 3 patients recovered, 2 with the use of the sulfonamides and 1 following operative evacuation of an abscess.

More,² in 1943, reported a case of meningitis due to a Friedländer bacillus in a twenty-six-month-old infant, with recovery following sulfonamide therapy.

In February, 1945, the favorable effects of streptomycin in experimental infections with micro-organ-

isms of the Friedländer group were reported.³ In November of the same year Herrell and Nichols⁴ discussed the clinical use of streptomycin in a study of 45 cases in which bronchiectatic involvement by the Friedländer bacillus was treated by aerosol and intramuscular injection of streptomycin.

It is apparent that, although streptomycin is being employed with increasing frequency, experience with the drug is limited. In the following case a patient with recognized meningitis due to Friedländer bacillus Type B was treated by intravenous and intrathecal injections of streptomycin. The clinical findings indicated an unmistakable, overwhelming meningitis, but evidence of such an infection was entirely absent grossly and almost so microscopically at the time of death.

CASE REPORT

F. M., a 49-year-old married man, was admitted to the hospital on July 30, 1945, with a diagnosis of a right-frontal brain tumor.

The past history indicated that he had not felt vigorous for 25 years. Seven years before admission he had been hospitalized for 8 months at the Veterans Administration Facility at Rutland Heights, Massachusetts, because of tuberculosis but no evidence of activity had been found. About 4 years later he began to have right-sided headache and difficulty in vision involving the right eye and to experience pins-and-needles sensations in the left hand and arm. Two and a half years before admission he had had a spell of unconsciousness during the night, and the spells had recurred at intervals of about 3 months until 5 weeks before admission, since then there had been three seizures. An aura, in the form of restlessness, was experienced preceding the convulsions. On one occasion there had been urinary incontinence. In 1944 the patient had been hospitalized at the Soldiers' Home in Chelsea, Massachusetts, at the Veterans Administration Facility, Bronx, New York, and at the Boston City Hospital. During 1945 he had been at the Veterans Administration Facility at Mt. Alto Washington, D. C., and at the Veterans Administration Facility, Rutland Heights, Massachusetts. During these earlier periods of hospitalization two encephalograms and a ventriculogram had been done.

*From the Veterans Hospital West Roxbury, Massachusetts. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the authors.

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On admission the patient complained of head pain and of difficulty in co-ordination of the eyes and hands. He had a feeling as though his head were being pulled to the right and backward. He was conscious of difficulty in memory and cerebrated more slowly than usual. He had also been conscious of increasing irritability during the preceding 2 months.

Physical examination showed a well developed and well nourished man 71½ inches tall and weighing 151 pounds. Two ventriculographic buttons were palpable in the skull. There was uncertainty in gait. The head intermittently and involuntarily twisted, the chin turning to the left and the occiput far to the right. There was considerable rhythmic tremor of the musculature, particularly about the shoulder muscles. The eye pupils, fields and fundi were normal. The breath sounds were harsh, but the heart sounds were normal. The pulse was 76, and the blood pressure was 124/80. Examination of the abdomen and extremities was negative, and the reflexes were physiologic.

Prior to operation the blood Wassermann and Mazzini reactions were negative. The hemoglobin was 16.9 gm and the white-cell count was 7100. Urinalysis was negative for sugar, albumin and organized pathologic elements. The sedimentation rate was 15 mm in 1 hour. The coagulation time was 3¼ minutes, and the bleeding time 1¼ minutes.

X-ray study on August 2 disclosed that the apex of the right lung was obscured. There was evidence of fibrosis and calcification above the level of the 2nd rib anteriorly, most marked in the extreme apex. These changes suggested parenchymal infiltration, apparently of long duration, with no evidence of recent changes. The remainder of the lung field was clear, with no changes in the cardiac silhouette. There was a slight bulge of the aortic knob. The changes in the right upper lung were suggestive of a tuberculous process. X-ray examination of the skull revealed areas with a somewhat circular appearance on both sides of the median line, apparently in the occipital region. It was impossible to state whether or not these findings were due to trephining or to bone erosion. No other abnormalities worthy of note could be made out. There was no indication of any definite lesion. The blood-vessel markings and the sutures disclosed no variations.

On August 13 a ventriculogram showed absence of filling of the anterior horn of the right ventricle. There was slight displacement of the ventricular system to the left.

On that day a craniotomy was performed by Dr. Gilbert Horrax and his associates, and a meningioma was removed from the right hemisphere in the frontal area. On the following morning the pulse, which had been under 90, had climbed to 120, the temperature was 102.2 and, later that day, 103.2° F, and the respirations were 35 per minute. From that time on until the time of death the patient ran a spiking febrile course, the temperature receding to normal only on August 18, and for the most part spiking to 103° F. The pulse and respiration were proportionately elevated. On the 3rd hospital day the patient complained of soreness on swallowing. Three days later he complained of a sore throat and a small grayish membrane was observed in the right tonsillar fossa. A throat culture was reported as showing the following organisms: gram-positive, lancet-shaped diplococci, with the appearance of pneumococci, short-chain, nonhemolytic streptococci, staphylococci, and gram-negative, encapsulated diplobacilli, with the appearance of Friedländer bacilli.

On August 20 lumbar puncture was done and 15 cc of xanthochromic fluid was removed under pressure. On the following day the patient was noted to be less alert, he was hypersensitive to touch and less rational. On that day 20 cc of definitely cloudy fluid was removed that contained 100 white cells and 5 red cells per cubic millimeter and had a sugar content of 16 mg and a protein content of 136 mg per 100 cc. A blood culture showed Friedländer's bacillus Type B, which was also demonstrated on spinal-fluid culture 2 days later. A definite diagnosis of meningitis was made and penicillin in doses of 20,000 units was given intramuscularly every 3 hours, as well as two intrathecal injections of penicillin, each containing 15,000 units. The patient received continued intramuscular and intrathecal penicillin, supplemented by 1 gm of sulfadiazine every 4 hours, through August 26. By that time he had become increasingly ill and markedly confused and disoriented and had developed paralytic ileus.

A spinal-fluid culture on August 24 eventually showed no growth. While the results of the culture were being awaited, however, the patient's condition became progressively worse, and it was believed that he could not possibly survive unless some heroic measures were instituted.

On the night of August 26 a dose of 0.05 gm of streptomycin was injected intracisternally at 10:00. At midnight 1.0 gm of streptomycin in 1000 cc of physiologic saline solution was given intravenously, and the same dose was repeated every 8 hours. Intracisternal injections of 0.05 gm of streptomycin were again given on August 27 and August 28. The spinal fluid, which on August 25 had become gelatinous to the point where only drops could be obtained even by suction, became less viscid. His condition seemed to be unchanged until the morning of August 29, when the patient's color suddenly became poor, the pulse more rapid and the respiration somewhat labored. Approximately 2 hours later he suddenly became pulseless and slightly cyanotic and within a few minutes stopped breathing. He was pronounced dead at 11:15 a.m.

Autopsy. At post-mortem examination, performed on August 29, the significant findings were confined to the lungs and brain. The immediate cause of death was represented by small coiled emboli in the branches of both pulmonary arteries. Although the source of these clots was not identified, it was assumed that they came from the small veins of the leg. The apex of the right lung was occupied by an extensive old dense scar. In the upper part of the right lower lobe there was a group of small abscess cavities averaging about 1 cm in diameter and having ragged walls and purulent contents. Adjacent to these cavities the parenchyma of the lung had a tough, grayish-yellow appearance, suggesting an organized pneumonia. The left lung was essentially normal, except for the emboli and some emphysematous blebs.

Microscopically, the right apex showed old dense collagenous tissue, with anthracotic pigment and a few surviving alveoli lined by cuboidal cells and containing phagocytes with foamy cytoplasm. There was also much peribronchial fibrosis, with scattered lymphocytes. The walls of the abscesses were fairly dense and fibrous, the exudate within them showing striking evidence of healing, with a predominance of large macrophages having a finely vacuolated cytoplasm (Fig. 1). There were also a few lymphocytes, plasma cells

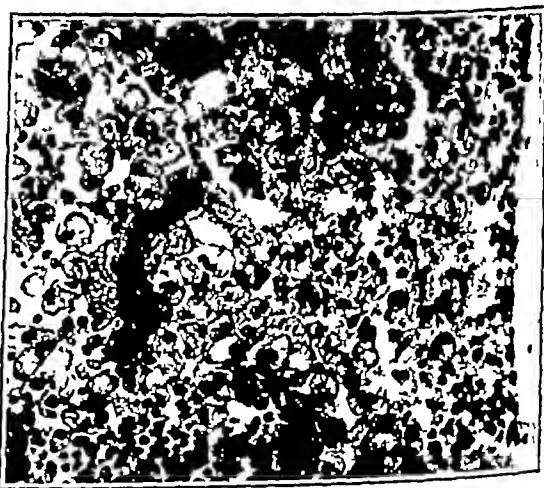


FIGURE 1 Photomicrograph of Wall of Pulmonary Abscess (phosphotungstic acid-hematoxylin — $\times 400$)

The exudate is composed largely of phagocytes, with foamy cytoplasm, and a few lymphocytes and polymorphonuclear leukocytes.

and polymorphonuclear leukocytes. Careful examination of sections stained by Giemsa's method revealed no bacteria. In the area of the abscesses there was an organizing pneumonia with a similar type of exudate.

The operative wound in the brain appeared clean, and the leptomeninges of both brain and spinal cord were grossly thin and delicate. Microscopically, however, there was the picture of a healing meningitis. The meninges showed an apparently edematous fibrillar connective tissue, scattered through which there were relatively scarce cells, most of which ap-

peared to be large mononuclear cells or monocytes, many of them having indented nuclei and pink-staining cytoplasm without definite evidence of phagocytosis (Fig. 2), there



FIGURE 2 Photomicrograph of Meninges (hematoxylin and eosin — $\times 400$)

Note the scattered mononuclear cells

were also a few lymphocytes. There was no acute polymorphonuclear reaction, and no bacteria were seen in the Giemsa-stained sections. The brain tissue appeared normal. Sections of the dura showed an organizing blood clot with a few polymorphonuclear leukocytes but no bacteria. There was some amorphous bluish-staining material suggesting fibrin foam. Unfortunately, the results of culture were not available.

The anatomical diagnoses were as follows: wound of recent operation (craniotomy for removal of meningioma), healing meningitis, pulmonary apical scars, healing pulmonary abscesses and resolving pneumonia (right lower lobe), pulmonary emboli (bilateral), and hydrothorax (bilateral).

DISCUSSION

On August 21 and again on August 23, Friedländer bacilli were cultured from the spinal fluid in this

case. In spite of the fact that spinal-fluid culture on August 24 showed no organisms, the facts remain that the spinal fluid became increasingly gelatinous subsequent to that day and that the patient's clinical progress was increasingly unsatisfactory. It is significant that after the administration of streptomycin the spinal fluid became less viscid and that at autopsy careful study of the meninges and of the surface of the brain disclosed evidence of a nearly healed meningitis. Whether such a finding might have presented itself with the continued use of penicillin alone is a question that cannot be answered. The complete disappearance of the extreme viscosity of the spinal fluid is regarded as having been due to the effect of streptomycin. It must be conceded that the absence of gelatinous accumulation and of any viscid accumulation was a surprising and dramatic finding. It may fairly be stated that this man did not die of a Friedländer-bacillus meningitis. His death was due to pulmonary embolism incident to a thrombophlebitis occurring in his lower extremities during the course of his illness.

SUMMARY

A case of Friedländer-bacillus meningitis treated with streptomycin administered intravenously and intrathecally is presented. The spinal-fluid changes during treatment and the complete absence of gross and the nearly complete absence of microscopical evidence of meningitis at autopsy are stressed.

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Correction. Several errors appear in the paper "Clinical Malnutrition in Italy in 1945" by Drs. Metcalf and McQueeney, which appeared in the September 26 issue of the *Journal*. In Table 2, under the heading "Anemia," both the third and fourth percentage figures should be changed from "43" and "57" respectively to "16," and in the second footnote, the number of cases should be changed from "70" to "258." In Table 3, under the same heading, the sixth percentage figure should be changed from "64" to "18.8," and in the second footnote, the second sentence should read, "Determinations made in 942 cases of the total population."

MEDICAL PROGRESS

OTOLARYNGOLOGY

CARLYLE G FLAKE, M D *

BOSTON

THE following summarized articles, which appeared in the literature on otolaryngology during 1945, were selected as being of general interest

THE EAR

Fenestration Operation

Fenestration of the labyrinth for the purpose of providing better hearing in otosclerosis is now a well established and widely performed operative procedure. Although many advances have been made in the technic of operation and the proper selection of patients, closure of the fistula by the formation of new bone remains the current post-operative bugbear.

With the latest modification in his technic, Lempert¹ believes that he has solved the two major causes of previous failure—osteogenic closure of the newly created vestibular fenestra and damage to the organ of Corti by postoperative serous labyrinthitis. The modification consists of placing a cartilage stopple in the fenestra, the cartilage, which is obtained from the spina helix, is regarded as ideal for the purpose, since it is smooth, inert and nonirritating to the endolymph and yet hard and tough enough to block osteogenesis in the bony rim of the freshly cut window and sufficiently light and elastic to transmit sound impulses efficiently. Fifty patients selected because of satisfactory evidence of good cochlear-nerve function were operated on, so that operative success and failure alike could, with fairness, be traced solely to the operation itself. The results were reported as 100 per cent successful. Partial or total closure of the fenestra had occurred in 140 of the 1000 patients operated on by Lempert during the previous seven years. Eighty-eight of these closures took place in the first 300 cases, in which fenestration was done in the prominence of the external semicircular canal. In the last 700 cases, in which the fenestra was made in the surgical dome of the vestibule, fifty-two closures occurred.

Day² reports that the operation is extremely difficult and tedious, usually requiring two and a half to three and a half hours. Moreover, the procedure is not bloodless, painless or devoid of danger. Since it is a purely mechanical method to create a new pathway for the transmission of sound waves to the

cochlear end organ, it does nothing toward removing or eliminating the otosclerotic foci and does not restore lost nerve function. Despite many failures, however, brilliant results have been achieved in restoring practical conversational hearing to an increasingly large number of persons with otosclerotic deafness. An analysis of the results of the operation in cases submitted to the Otosclerosis Study Group reveals that in 211 cases in which the original operation, which involved the horizontal semicircular canal, was performed, improved hearing followed in only 47 per cent, and hearing reached a satisfactory level of understanding of normal speech in only 10 per cent. With the revised operation, in which the window is created in the roof of the vestibule, 76 per cent of 554 patients had improved hearing, but in only 31 per cent did the hearing reach the practical level. The only justifiable purpose for the operation is to restore practical conversational hearing, and cases reported as successful should be limited to those in which the hearing reaches this level. The practical level of hearing for normal conversation is somewhere around the level of 25 decibels. Therefore, if a patient has a loss of 70 decibels and the operation gives him a 30-decibel improvement, he is still unable to understand normal speech and the operation should not be considered successful. Not more than 10 per cent of patients with otosclerosis are considered suitable for the operation, which should be reserved mainly for adolescents and young adults. Patients over forty years of age usually have secondary nerve degeneration that prevents their hearing from reaching a practical level after operation. Good bone conduction is regarded as essential, since hearing loss by bone conduction indicates nerve damage and cannot be restored by operation. A hearing aid is preferable to operation in cases in which a high postoperative hearing level cannot reasonably be expected to result. In Day's series of 75 cases, a good result with practical hearing for conversation was obtained in 40, or 74 per cent, of 54 patients operated on between October, 1941, and June, 1944. In 3 cases the fenestra closed but was successfully reopened, making a total of 43, or 80 per cent, with successful results. Average hearing loss for the speech range for pure tones before operation was 48.2 decibels. Following operation, there was an average improvement of 28.5 decibels and an average hearing loss in the speech range of 19.7 decibels.

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The conclusion was reached by Berry³ that a well fitted hearing aid could give greater sound amplification and furnish help to a wider group of patients at the cost of less pain and worry than could a fenestration operation. On the premise that hearing for speech is more important than hearing for pure tones, as measured by standard audiometers, Shambaugh⁴ retested Berry's conclusions and surveyed a group of patients on whom the fenestration operation had been performed after the use of hearing aids, to get their impression of the comparative benefits. The testimony was predominantly in favor of the operative result. According to Shambaugh, the hearing aid shows to best advantage under standard test conditions—that is, in a soundproof room in which there is little interference of static, distortion and amplification of outside noises, all of which combine to hamper the hearing for speech. So that subjective impressions might be ruled out, 14 patients, each of whom had worn a hearing aid before operation and had been tested by means of a speech audiometer, with and without the aid, both before and after fenestration operation, served as the basis for the following conclusion: patients with an average gain (20 decibels or more with the pure-tone audiometer) in hearing after the fenestration operation had better hearing for speech than they had with hearing aids before operation, and those who obtained less than the average gain in hearing for pure tones were not benefited. On the basis of one-year results with the fenestration operation as it is now used, the further conclusion is reached that the ideal subject for the fenestration procedure has about a 90 per cent chance of securing permanently better hearing and a 70 per cent chance that the hearing will be as good as, or better than, it was with a hearing aid.

Congenital Deaf-Mutism

Carruthers⁵ reports that in Australia, especially during the years 1940, 1941 and 1942, an exanthematous disease, believed to be rubella, occurred in widely scattered parts of the country. There was a greater tendency than usual for adults, and especially young adults, to contract the disease. A proportion of pregnant women had this disease, which, although minor for the mother, had disastrous effects on the developing fetus, as revealed at birth. Congenital cataracts, cardiac defects and anomalies, deaf-mutism, microcephaly, general stunting of the growth and dental defects were reported. The stage of pregnancy at which the infection occurred was apparently most important in influencing the type and extent of congenital defects. If infection occurred during the first six weeks, fetal damage was widespread, including the eyes, both divisions of the ears, the heart and perhaps many other organs. After the sixth week the eyes sometimes escaped, the heart was spared and the semicircular canals developed normally, but the

cochlea was still likely to be damaged and growth was sometimes retarded. After the third month damage to the fetus was rare. Apparently there was no correlation between the severity of the infection in the mother and the degree of fetal damage. Since deafness is often not discovered until it is evident that speech development is retarded, it is not yet possible to state exactly what proportion of children born of mothers who had rubella during pregnancy have severe hearing defects, although it is likely that the figure is over 50 per cent. Of 102 children with congenital defects whose mothers were known to have had rubella during pregnancy, 74 were deaf and 14 of these also had congenital heart lesions. The most frequent type of congenital anomaly in deaf-mutism is that in which the middle ear and the bony form of the inner ear are normal and the vestibule and semicircular canals are more or less normal in development but in which the cochlea, especially Corti's organ, and the saccule show evidence of maldevelopment. Congenitally deaf-mute infants whose deficiency is the result of maternal rubella belong to this group, for these patients are quite deaf but not completely insensitive to sound and, so far as they have been tested, give evidence of an active, although reduced, vestibular apparatus. Many children gave evidence of loss of hearing over the tone range 512 to 2048. Tests of caloric labyrinthine reactions in 9 cases showed slightly reduced responses as compared to normal. An interesting feature of the test was absence of sickness from caloric stimulation, even when a pronounced nystagmus was induced. By contrast with the gross inactivity of the cochlea, it is obvious that often the semicircular canals were largely spared. In the series of Carruthers 17 deaf-mute children were under observation, the oldest of whom was six and a half and the youngest three and a half years. At the age of three and a half years several children began to use their hearing. It is hardly possible that the receptive function of the inner ear actually developed, rather, it is believed that the children began to take some interest in their residual powers as a result of mental growth and training. Parents are instructed to use every means to preserve the baby voice until such a time as special training is practicable.

Pregnancy and Otosclerosis

Allen,⁶ in a review of the literature regarding the possible etiology of otosclerosis, discussed the effects of pregnancy on deafness, as observed in 18 cases without audiograms, including 13 by personal communication and 5 from the literature, and 54 cases with audiograms, including 19 by personal communication and 35 from the literature. No change in hearing occurred in 24 cases without and in 8 with audiograms. The otologists believed that decrease in hearing was consistent with that which

MEDICAL PROGRESS

OTOLARYNGOLOGY

CARLYLE G. FLAKE, M.D.*

BOSTON

THE following summarized articles, which appeared in the literature on otolaryngology during 1945, were selected as being of general interest.

THE EAR

Fenestration Operation

Fenestration of the labyrinth for the purpose of providing better hearing in otosclerosis is now a well established and widely performed operative procedure. Although many advances have been made in the technic of operation and the proper selection of patients, closure of the fistula by the formation of new bone remains the current postoperative bugbear.

With the latest modification in his technic, Lempert¹ believes that he has solved the two major causes of previous failure—osteogenic closure of the newly created vestibular fenestra and damage to the organ of Corti by postoperative serous labyrinthitis. The modification consists of placing a cartilage stopple in the fenestra; the cartilage, which is obtained from the spina helcis, is regarded as ideal for the purpose, since it is smooth, inert and nonirritating to the endolymph and yet hard and tough enough to block osteogenesis in the bony rim of the freshly cut window and sufficiently light and elastic to transmit sound impulses efficiently. Fifty patients selected because of satisfactory evidence of good cochlear-nerve function were operated on, so that operative success and failure alike could, with fairness, be traced solely to the operation itself. The results were reported as 100 per cent successful. Partial or total closure of the fenestra had occurred in 140 of the 1000 patients operated on by Lempert during the previous seven years. Eighty-eight of these closures took place in the first 500 cases, in which fenestration was done in the prominence of the external semicircular canal. In the last 700 cases in which the fenestra was made in the surgical dome of the vestibule, fifty-two closures occurred.

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drum were thoroughly cleaned and dried and the canal wall and drum membrane were sprayed with a coating of sulfanilamide. Every four hours 1 gm of sulfathiazole was administered, and if no improvement was noticed, the dose was increased to 1.5 gm every four hours. If sulfathiazole was not tolerated, sulfadiazine was used. This routine, which was continued until the discharge, edema and itching subsided, was successful. The average duration of treatment in this series in a tropical climate was less than seven days.

Radium Therapy for Aerotitis

Irradiation of the nasopharynx by radium for the control of aerotitis proved to be safe and effective prophylaxis and treatment as used by the United States Army Air Forces.¹² The flying personnel treated numbered 6881, but owing to the shifting of personnel only 1129 men were available for observation thirty days or more after the completion of the therapy. The conclusions reached are based on the study of this group. Seventy-four per cent of 636 men with a history of recurrent aerotitis had less difficulty in ventilating their ears during flights. Eighty-nine per cent of the same group showed a marked decrease in the amount of nasopharyngeal lymphoid tissue when examined with a nasopharyngoscope thirty days or more after the third treatment. The beneficial effect of prophylactic irradiation was shown by the drop in incidence of aerotitis in 778 men after high-altitude flights. Following the completion of treatment, the incidence of aerotitis in this group was reduced from twice that in a control group of 922 men with normal nasopharynges to a level almost identical with that in the control group. The principal cause of failure to improve after irradiation treatment was the presence of a large mass of adenoid tissue. For such patients, surgical removal, supplemented by irradiation, would have been more effective. Other contributing factors to failure of treatment were considered to be nasal allergy, chronic sinusitis and psychologic reactions. Treatment consisted in placing two nasopharyngeal applicators, each containing 50 mg of radium sulfate, in the nasopharynx for a period of eight and a half minutes. From one to three treatments were given at intervals of eight days. In 14,045 treatments there was not a single case of burn or ulceration of the nasopharynx or nasal mucous membrane.

Surgery of Facial Nerve

Tickle¹³ reports his observations on 300 operations for peripheral facial paralysis performed since 1930. When interruption of the continuity of the nerve was due to trauma, fresh nerve grafts from the anterior femoral cutaneous nerve were used to bridge the gap. Grafts from either motor or sensory nerves may be employed, but the latter are regarded as preferable. Two types of nerve injury respond to

surgery: trauma to the facial nerve and Bell's palsy. Patients with facial paralysis following trauma should be tested daily with the faradic current. So long as any response occurs, operation should be deferred, but if reaction to the faradic current is lost, the nerve should be investigated immediately. In Bell's palsy, 85 to 90 per cent of patients recover, the remainder can be helped by decompression of the nerve if this is done soon after the onset. As in trauma, the same criteria apply for determining the time to operate. Patients who retain response to the faradic current recover, those who lose this response may never, or only partially, recover. If response to galvanic stimulation is lost in either type of case, operation is useless, for this means atrophy or fibrosis of the facial musculature.

NOSE AND SINUSES

Chemotherapy

Kern¹⁴ condemns the use of sulfonamides in the common cold because of the risk of inducing sensitivity to a drug that may later be required in a more serious infection. Furthermore, the doses employed are usually inadequate to prevent pneumonia, and yet this inadequate dosage can be responsible for a drug-fast strain of the pneumococcus. Administration of these drugs renders the pneumococcus untypable and thereby prevents the use of specific serum therapy in patients with drug-fast pneumococci. Routine administration of the sulfonamides, which may interfere with the development and maintenance of a desirable active immunity to a number of frequent pathogenic organisms, may increase the incidence of pyogenic complications in the respiratory tract in the period immediately following the cold.

Hayden and Bigger¹⁵ gave sulfanilamide lozenges, each containing 0.065 gm of the drug, to a group of troops in an Army training center. A similar group were given lozenges of the same base but lacking the sulfanilamide. The lozenges were administered five times daily for sixteen days. From the observations on these groups, it was concluded that if the sulfanilamide lozenges afforded any protection against colds, it was of such an insignificant degree as to be not worth the trouble, expense and risk involved.

In the treatment of acute sinusitis and its complications, Hauser and Work¹⁶ favor the intramuscular injection of 20,000 units of penicillin every three hours until the optimum result has been obtained. In the treatment of orbital cellulitis, this therapy has replaced every other method of treatment. In the presence of allergic rhinitis with superimposed infection, penicillin therapy eliminates all evidence of suppuration but produces no change in the underlying allergy. The results obtained in chronic sinusitis depend to a large extent on the duration of the disease. When the duration is relatively short, a cure can be accomplished by the in-

might be expected during the normal progress of the disease. Hearing was decreased beyond normal expectancy in 30 cases without audiograms and in 5 with audiograms. In 4 cases deafness first occurred during pregnancy. For progressive deafness to be considered an indication for therapeutic abortion, a definite diagnosis of otosclerosis must first be made. The hearing should be followed carefully before, during and following pregnancy and lactation for evaluation concerning succeeding pregnancies. Otosclerosis should not be considered as an indication for therapeutic abortion in primiparas. A familial history of deafness need not be present and yet may be one of the deciding factors in the decision to interrupt a pregnancy. A multipara may have considerable right to question the continuation of her pregnancy, if accurate otologic evidence obtained at previous pregnancies has shown a marked, sustained loss of hearing. Before therapeutic abortion is decided on, the patient should be informed that otosclerosis is a progressive disease, even without pregnancy, and that hearing aids and lip reading offer considerable help.

Barton⁷ made a study of the effect of pregnancy on the hearing of 133 women who were known to have otosclerosis and who had one or more pregnancies. In 73 patients the hearing was made worse by pregnancy, and in 51 of these the hearing loss occurred during the first pregnancy and persisted in all but 2 of the patients. In multiparas who experienced loss of hearing with the first pregnancy, about 50 per cent showed no further loss with subsequent pregnancies. It was concluded that therapeutic abortion or sterilization is not indicated in women with otosclerosis, since the hereditary nature of the disease has not been conclusively proved and the unfavorable effect of pregnancy on the hearing is not constant.

Penicillin in Otolaryngology

Johnson and his associates⁸ report a series of 23 cases in which a simple mastoidectomy was performed for suppurative mastoiditis following scarlet fever or measles. The mastoid wound was sutured, penicillin being applied to the cavity through a urethral catheter. The recommended dose of the drug was 10,000 units every eight hours for four days. Seventeen patients showed a complete cure after one course of treatment, whereas 6 remained well after a second course. When penicillin was given in adequate dosage, healing of the postaural wound and a dry external auditory canal usually occurred on the fifth postoperative day. If aural discharge recurred, the catheter was reinserted and more penicillin was injected until the ear had completely cleared. Local treatment with penicillin seems preferable to the use of sulfonamides when susceptible organisms are present, because of the absence of any harmful toxic effects, the slight risk of sensitization and the increased speed of healing.

Allman⁹ used penicillin intramuscularly in 511 cases of otitis media caused by scarlet fever. Twenty-seven cases of scarlet-fever mastoiditis were cured in this manner without surgery. In 33 cases of mastoiditis due to scarlet fever, penicillin was used both intramuscularly and locally, these cases required surgical exenteration of the mastoid. Meningitis occurred in 2 patients. In the postoperative treatment of 14 cases of non-scarlet-fever mastoiditis, penicillin was administered by the same method. Ten of these patients had acute and 4 had chronic mastoiditis. Administration of the drug by the intramuscular route was accomplished by giving 20,000 units at the onset and following this by 10,000 units every three hours thereafter day and night until the tympanic membrane and the postaural incision were healed. For local application within the mastoid cavity, 10 cc of a solution containing 500 units of penicillin per cubic centimeter was instilled into the mastoid cavity every four hours when the cavity was large, and 5 cc when it was small. Sodium penicillin was used. The postaural incisions healed by primary intention. Administration of penicillin from the onset of scarlet fever reduces the incidence of ear complications. In a study of 300 patients with scarlet fever in the wards in which no penicillin was administered, acute otitis media developed in 10.9 per cent, whereas in wards in which penicillin was administered, the incidence in 300 cases of scarlet fever was only 5.6 per cent.

Otitis Externa

Senturia's¹⁰ studies on external otitis at Randolph Field, Texas, show that fungi play little part in the inception or persistence of external otitis. Gram-negative bacilli, especially those of the *Pseudomonas* group, were found in a high percentage of cases showing acute desquamative and chronic suppurative external otitis, but no single organism or combination of bacteria occurred frequently enough to be considered a specific cause of external otitis. Bacterial infection produces almost any type of discharge, from a thin serous type to a thick, grayish, purulent secretion. The so-called "blotting-paper" discharge is not pathognomonic of fungus infection. It was concluded that, since no single available chemotherapeutic agent is an effective bactericide and fungicide for use in acute infections of the ear canal, careful examination and observation of all types of external otitis are necessary.

In a series of 90 cases of otitis externa in a tropical climate studied by Simon,¹¹ only 20 per cent showed cultures yielding a fungus. The presence of an organism in culture from otitis externa does not absolutely imply that the organism is the primary agent, it may or may not be the one producing the lesion. In each of the 90 cases, a bacterial growth on culture was obtained, and it was concluded that bacteria are the primary invaders in this disease. In the last 60 cases the external auditory canal and

hemorrhagic inflammation of the soft palate was observed

Nevert²² reports that, with rare exceptions, observations to date suggest that one of the most important factors in late post-tonsillectomy hemorrhage is the reduction of the prothrombin of the blood brought about by the use of acetylsalicylic acid or salicylates. This reduction in prothrombin interferes with coagulation. With the simultaneous administration of Synkavite, a compound similar to vitamin K, the prothrombin-lowering effect of acetylsalicylic acid is overcome and normal coagulation can take place. Rectal suppositories and tablets composed of 0.3 gm of acetylsalicylic acid and 5 mg of Synkavite were used. Suppositories were given to 173 patients, and the tablets to 110 patients. The results were reported as most gratifying, late tonsillar bleeding occurring in only 4 patients among the total of 283 — an incidence of 1.4 per cent. When compared with an incidence of late tonsillar hemorrhage of almost 10 per cent accompanying the former routine, which called for the free use of salicylates alone, the present results demonstrate that proper postoperative care should include measures designed to prevent lowering of the prothrombin content of the blood. It is concluded that salicylates should either be avoided or, if given, combined with a drug such as Synkavite, which prevents hypoprothrombinemia.

Sulfathiazole in Chewing Gum

In treating a series of patients who had infections of the mouth, tonsils or pharynx, Fox and his associates²³ used a tablet of gum containing 0.25 gm of sulfathiazole. One tablet was administered every three hours, except when a severe infection of the throat was present, when the patient was instructed to chew the tablet for an hour and to rest for an hour. In 32 cases of acute lymphoid pharyngitis and follicular tonsillitis, 72 per cent showed a decided decrease in total bacterial counts of cultures made from mouth washings within forty-eight hours, along with complete disappearance of the beta-hemolytic streptococcus from the cultures. In 38 cases of ulcerative stomatitis, a decrease in the total bacterial count was noted in 67 per cent, with a 75 per cent decrease in the beta-hemolytic streptococcus within forty-eight hours. Even more spectacular was the rapid clinical resolution of these conditions. The same results were obtained in the Plaut-Vincent ulcerative type of stomatitis. In chronic mouth conditions, such as salivary adenitis and catarrhal stomatitis, associated with mouth breathing in persons with hyperplastic pansinusitis, a decrease in the total bacterial count was also noticed. Clinical improvement, as demonstrated by the disappearance of mouth odor and coated tongue, was observed. It was concluded in this preliminary report that, from the standpoint of minimal systemic toxicity and maximum local

antibacterial potency, sulfathiazole in chewing gum is the preferable local chemotherapy for infections of oral and pharyngeal mucosa that are susceptible to the sulfonamides. The best clinical results were obtained in conditions of the mouth and pharynx in which the beta-hemolytic streptococcus was the predominant organism.

LARYNX

Hoarseness

Zinn²⁴ points out that hoarseness may result from inflammatory infections of the larynx, trauma, tumors and disturbances of the central and peripheral nervous systems. The diagnosis of functional hoarseness should not be made until all organic lesions have been excluded. This condition requires as careful study and treatment as if a definite lesion were present. It is now generally conceded that 80 per cent of all cases of carcinoma of the larynx are curable by operation if the diagnosis is made while the disease is still intrinsic. In a previously reported series of 25 cases of total laryngectomy, 80 per cent of the patients gave a history of preoperative hoarseness for periods varying from six months to over two years. In another series of 178 cases, hoarseness was a constant symptom, but 100 of the patients, who were not referred until all classic symptoms of carcinoma were present, had to be classed as inoperable. Of 144 cases of carcinoma of the larynx recently examined, 134 patients (93 per cent) gave a history of hoarseness as the first symptom. Jackson and Jackson²⁵ report statistics on 410 cases, in which hoarseness was an early symptom in 95 per cent. Negus²⁶ urges that no patient be continuously hoarse for more than three weeks without laryngeal examination and diagnosis.

Cancer of the Larynx

According to Tucker,²⁷ in a large number of cases surgical cure of cancer of the larynx by laryngofissure and total laryngectomy has been reported, and it is his belief that surgery is the method of choice in the treatment of this condition when adequate excision can be performed. Surgical excision by laryngofissure should give a permanent cure in from 80 to 85 per cent of cases in early intrinsic cancer. In more extensive lesions in areas of the larynx where metastatic extension is more rapid, total laryngectomy is required, and a cure of from 50 to 60 per cent of advanced cases of this type may be expected. When the lesion has extended beyond the cartilaginous framework of the larynx, wide excision of the involved area with removal of the larynx, followed by postoperative irradiation, offers a fair prognosis — possibly 30 to 50 per cent of the patients are cured. The possibility of late recurrence of cancer in the regional lymph nodes, without local recurrence in the larynx, following laryngofissure or local recurrence in the pharynx or trachea following laryngectomy must be kept in

tramuscular injection of penicillin alone. In chronic suppurative disease of the sinuses of long duration, penicillin alone is of little value, but when used in conjunction with adequate sinus surgery, rapid and complete cures were accomplished.

Sinus Disease in Children

According to Taquino,¹⁷ two facts are generally overlooked in sinus disease in children: that it is frequent and that it is often of allergic origin. Diagnosis presents some difficulty because of the age of the patient and the size of the nasal passages. Transillumination of the sinuses is regarded as unreliable, and even radiologic information may be misleading. The same diagnostic procedures that are employed in adults should, however, be carried out in children for the diagnosis of sinus disease. In general, treatment should be of a conservative nature. Removal of the tonsils and adenoids should not be done unless definitely indicated. The routine use of chemotherapy is undesirable. The type of organism found in the sinuses should indicate the chemotherapeutic agent to be employed. Whenever drainage of the sinuses is necessary, it should be carried out by the simplest method. Sinus disease of allergic origin must be treated primarily as an allergy. In both types of sinus disease, attention to the general health is of the greatest importance.

Frontal-Sinus Surgery

In a series of 123 cases in which the Lynch operation for chronic infection of the frontal and ethmoidal sinuses had been performed, Goodale¹⁸ reports that reoperation was necessary in approximately 30 per cent. At the second operation, the causes for failure were noted as follows: obstruction of the nasal frontal passage by adhesions, remnants of the frontal-sinus floor that had given rise to undrained infected pockets in the frontal sinus, and incomplete ethmoidectomy, especially failure to remove orbital extensions of the ethmoid. To maintain the patency of the opening between the frontal sinus and the nasal cavity, a strip of tantalum foil, 1.5 cm. wide and 4.0 cm. long, was sutured by means of fine tantalum wire to the orbital periosteum, at about the position of the pulley. During the previous two years, this technic had been used with excellent results in a total of 8 patients.

PHARYNX AND TONSILS

Monilial Pharyngitis

Tumulty and Michael¹⁹ report a series of 18 patients with monilia infection of the oropharynx. Although the disease usually occurs in undernourished infants or debilitated adults, the patients reported were well nourished young men in good general health. There is no clinical feature of monilial pharyngitis that helps to differentiate it from streptococcal pharyngitis or from pharyngeal diphtheria. Secondary syphilis and Vincent's angina

may also cause some confusion. The diagnosis is made by direct examination of mucosal scrapings and by culture material obtained from diseased sites. Throat swabs should be planted on slants of Loeffler's medium. If monilia are present, small creamy colonies appear after twelve to eighteen hours of incubation. Overnight growths are stained with Loeffler's methylene blue, and either monilia or diphtheria organisms can be demonstrated by this method. In 5 of the cases reported, monilia was considered solely responsible for the acute pharyngitis. In 3 other cases, its significance could not be determined owing to the presence of beta-hemolytic streptococci. In the remaining cases, it was believed to have had no etiologic role.

Poliomyelitis and Recent Tonsillectomy

Anderson²⁰ reports that a severe epidemic of poliomyelitis occurred in Utah in 1943. Of the hospitalized patients, 31.6 per cent had the bulbar or bulbospinal type. A state-wide survey showed the number of tonsillectomies performed to be 1411 in July, 2111 in August and 677 in September. Seventeen of these children developed poliomyelitis within thirty days after operation; all the patients had either the bulbar or bulbospinal type of poliomyelitis. During the same three-month period, 261 cases of poliomyelitis were reported in the state, in which 232 patients were children between the ages of three and sixteen. The incidence of poliomyelitis in the tonsillectomized group was 0.40 per cent, or about two and a half times greater than the 0.15 per cent incidence of poliomyelitis in the child population of the same age group. The total number of bulbar or bulbospinal cases of poliomyelitis in children three to sixteen years of age was 39, and 17 (46 per cent) of these cases had been preceded by a recent tonsillectomy. A comparison of the incidence of bulbar cases in the general child population with the incidence in the tonsillectomized group showed that, during this epidemic, the possibility of contracting bulbar poliomyelitis was sixteen times greater in children immediately after tonsillectomy than in children in the general population.

Post-Tonsillectomy Hemorrhage

According to Singer,²¹ post-tonsillectomy hemorrhage occurs in 5 to 10 per cent of all tonsillectomized patients. In the clinics and hospitals of Central Europe, the incidence of this complication is practically nil because of the practice of giving aminopyrine instead of acetylsalicylic acid. A comparison of the preoperative and postoperative regimes used in this country and abroad show this to be the only significant difference. In 75 patients observed during 1943 who, after tonsillectomy, were placed on an acetylsalicylic acid-free post-tonsillectomy routine, no secondary hemorrhage occurred and, what is regarded as more significant, no case of

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

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FOUNDED BY RICHARD C. CABOT

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CASE 32451

PRESENTATION OF CASE

First admission. A seventy-four-year-old man entered the hospital because of gross urinary bleeding of two weeks' duration. The bleeding was painless and there were no other symptoms. On examination, the left lobe of the prostate was slightly enlarged and firm, the left testicle was atrophied, and there was a reducible left inguinal hernia. Cystoscopy revealed a small, sessile growth with superficial papillary projections located deep in the left ureteral orifice. Treatment consisted in cutting away the tumor in pieces and implanting four radon seeds of 1 millicurie each. The pathological report was carcinoma (Grade III). The patient was discharged on the eleventh day.

Final admission (four years and six months later). During the period following operation, the patient visited the Out Patient Department every six months. The bladder wound healed, leaving a white scar. No recurrence was apparent at any time. The lateral lobes of the prostate became slightly enlarged and more indurated. There was slight inflammatory edema of the bladder outlet. Two years before admission the patient began to be constipated. Approximately six months before admission he began to notice bright-red blood in the stools, continuing until admission, the stools were never black. About a month later he noticed a small painless lump in the right neck that had progressed to 3 cm. in diameter by the time of entry. The patient believed that he had begun to lose ground about a month before admission. His

appetite failed, and he lost all sensation of taste. He had lost 15 pounds in weight during the preceding year. The throat became dry and somewhat sore. A diffuse, dull, crampy epigastric pain unrelated to food and slightly relieved by soda annoyed him constantly. Blood was said to have appeared in the urine at about the same time. Three weeks before admission the skin turned yellow, and the jaundice subsequently deepened. The stools became light colored in the weeks before entry.

On physical examination the patient was thin and jaundiced and spoke with a hoarse voice. On the right side of the neck beneath the sternomastoid muscle was a mass, 3 by 4 cm. in diameter, that was hard and only slightly movable. The chest was clear. The liver extended 4 cm. below the ribs. There was a right indirect hernia, and the right testicle was atrophic. The right lateral lobe of the prostate was firm, with a poorly defined border.

The temperature was 98°F, the pulse 65, and the respirations 15. The blood pressure was 120 systolic, 60 diastolic.

Examination of the blood showed a hemoglobin of 12 gm. per 100 cc. and a white-cell count of 6050. The urine was bile stained, gave a ++ test for albumin and contained rare white cells per high-power field but no red cells. The stools were fluid, brown and grossly bloody. X-ray films failed to reveal metastases in the chest. No definite esophageal lesion was seen, but there was delay in the passage of barium through the lowermost portion of the esophagus where it crossed the aorta. The duodenal bulb was deformed in a manner characteristic of an old ulcer. The only abnormal blood values were a bilirubin of 17 mg. per 100 cc. direct and 20 mg. indirect, a prothrombin time of twice normal and a chloride of 97 milliequiv. per liter. The cephalin-flocculation test was + in twenty-four hours and ++ in forty-eight hours. The acid phosphatase level was 1 unit, and the alkaline phosphatase 163 Bodansky units per 100 cc.

On the day after admission generalized itching of the skin developed. In the next two weeks three diagnostic procedures were performed. Proctoscopy disclosed an obstructing tumor in the rectosigmoid, 14 cm. from the anus, biopsies from

mind, for metastatic lymph nodes have appeared from five to ten years after surgical excision of the primary lesion. The mass should be removed immediately by surgery, radon seeds implanted in the region from which the node was removed and x-ray irradiation applied to the neck. Jackson and Norris²⁸ use the following indications for surgical treatment of cancer of the larynx: lesions occupying the middle third of one cord are suitable for laryngofissure, lesions reaching the anterior commissure and even involving the opposite cord are also amenable to extirpation by the laryngofissure route, but in such cases the so-called "anterior-commissure" technic should be used, lesions in which the growth is cordal but has reached the posterior end of the cord and produced impairment of motility or has extended subglottically ordinarily call for total laryngectomy, as do lesions involving the ventricle or ventricular band, and lesions in which the tumor has invaded cartilage (but not muscle) also call for laryngectomy, provided there are no metastases—where there are metastases, combined laryngectomy and neck dissection should be done. Irradiation is regarded as preferable in lesions unsuitable for laryngofissure in which laryngectomy is contraindicated by the age, physical condition or temperament of the patient, and also for growths inoperable because of extrinsic origin or extension or because of cervical metastases. An analysis of the end results in a series of 150 patients with cancer of the larynx treated at the Temple University Hospital by surgery and irradiation from 1930 to 1937 inclusive showed a combined five-year cure rate of 64 per cent. Of 101 patients with intrinsic lesions who received surgical treatment by either laryngofissure or laryngectomy 80 patients, or about 75 per cent, obtained at least a five-year cure. Nine patients with extrinsic lesions, on whom laryngectomy was performed, died. During the same period, 34 patients were treated by irradiation (protracted fractional technic), 22 with intrinsic and 12 with extrinsic growths, in the former group, a 59 per cent and in the latter a 25 per cent five-year cure rate was obtained.

Hemangioma of the Larynx

Kasabach and Donlan²⁹ state that the possibility of hemangioma should be considered in infants when there is a history of recurring, obstructive dyspnea. The symptoms of hemangioma of the larynx in infants, in order of frequency, are obstructive dyspnea, inspiratory stridor, a hoarse cry, croupy cough, blood-tinged mucus, gross hemorrhage and fever, if there are pulmonary complications. Laryngoscopic examination shows a red or bluish subglottic mass. The presence of other hemangiomas on the body also helps to confirm the diagnosis. Hemangiomas of the larynx in infants are always subglottic, whereas in adults they are usually found on or above the vocal cords. In the treatment of

hemangioma of the larynx in infants, the dyspnea must first be relieved by low tracheotomy, radiation therapy is then begun, using either radium or x-ray. Two cases were reported in which x-ray therapy was used with good results, both children were normally developed and had adequate airways two years or more after the completion of treatment.

Recurrent-Nerve Paralysis

Laszlo and Fiertz³⁰ have been successful in determining the prognosis in cases of recurrent-nerve paralysis following thyroidectomy. The principle of examination follows the same underlying criteria as the electrodiagnosis of any other peripheral-nerve injury. The necessary equipment consists of an electrical apparatus that provides both a straight galvanic and a faradic current. A flat electrode is placed on the sternum and the nerve-testing electrode is put on the motor point for the vocal cord—that is, on the respective side of the Adam's apple. If a faradic response is obtained, the damage is minor and recovery can be expected in about two months. If, in the absence of any faradic response, the cathodal closing contraction is better than the anodal response, the second stage of the reaction of degeneration is present and recovery cannot be expected within less than nine months. If the formula is reversed, a complete reaction of degeneration is present and the outlook is accordingly worse. Whether or not the nerve has been anatomically severed cannot be determined by one examination alone, but if, after two months of biologically correct treatment, re-examination gives the same or a worse formula, the conclusion is that the nerve is cut and further conservative therapy is useless. If, however, the formula or the quality of the contraction has improved, treatment can be continued, although the time for recovery may require one and a half or two years. If no reaction whatever is obtained, the diagnosis is obvious and no benefit may be expected from electrotherapy.

300 Longwood Avenue

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Final admission (four years and six months later). During the period following operation, the patient visited the Out Patient Department every six months. The bladder wound healed, leaving a white scar. No recurrence was apparent at any time. The lateral lobes of the prostate became slightly enlarged and more indurated. There was slight inflammatory edema of the bladder outlet. Two years before admission the patient began to be constipated. Approximately six months before admission he began to notice bright-red blood in the stools, continuing until admission, the stools were never black. About a month later he noticed a small painless lump in the right neck that had progressed to 3 cm. in diameter by the time of entry. The patient believed that he had begun to lose ground about a month before admission. His

appetite failed, and he lost all sensation of taste. He had lost 15 pounds in weight during the preceding year. The throat became dry and somewhat sore. A diffuse, dull, crampy epigastric pain unrelated to food and slightly relieved by soda annoyed him constantly. Blood was said to have appeared in the urine at about the same time. Three weeks before admission the skin turned yellow, and the jaundice subsequently deepened. The stools became light colored in the weeks before entry.

On physical examination the patient was thin and jaundiced and spoke with a hoarse voice. On the right side of the neck, beneath the sternomastoid muscle, was a mass, 3 by 4 cm. in diameter, that was hard and only slightly movable. The chest was clear. The liver extended 4 cm. below the ribs. There was a right indirect hernia, and the right testicle was atrophic. The right lateral lobe of the prostate was firm, with a poorly defined border.

The temperature was 98°F, the pulse 65, and the respirations 15. The blood pressure was 120 systolic, 60 diastolic.

Examination of the blood showed a hemoglobin of 12 gm. per 100 cc. and a white-cell count of 6050. The urine was bile stained, gave a ++ test for albumin and contained rare white cells per high-power field but no red cells. The stools were fluid, brown and grossly bloody. X-ray films failed to reveal metastases in the chest. No definite esophageal lesion was seen, but there was delay in the passage of barium through the lowermost portion of the esophagus where it crossed the aorta. The duodenal bulb was deformed in a manner characteristic of an old ulcer. The only abnormal blood values were a bilirubin of 17 mg. per 100 cc. direct and 20 mg. indirect, a prothrombin time of twice normal and a chloride of 97 milliequiv. per liter. The cephalin-flocculation test was + in twenty-four hours and ++ in forty-eight hours. The acid phosphatase level was 1 unit, and the alkaline phosphatase 163 Bodansky units per 100 cc.

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which showed adenocarcinoma (Grade II) Aspiration biopsy of the mass in the neck was reported as showing "metastatic carcinoma consistent with bladder origin" Peritoneoscopy revealed a large blue-gray liver No metastases were seen in the liver or peritoneum Omentum adherent around the gall bladder prevented visualization of that region

On the twelfth, thirteenth, fourteenth and fifteenth days the temperature spiked to 102 to 103°F, with a shaking chill at each daily peak Painful effusion of the right knee developed on the fifteenth day A watery diarrhea, with partial incontinence, was the patient's major difficulty The jaundice persisted In the last three days the general condition deteriorated rapidly On the eighteenth day the patient became comatose and died a few hours later

DIFFERENTIAL DIAGNOSIS

DR PAUL ZAMECNIK I am curious about the occupation of this patient in view of the fact that carcinoma of the bladder is one of the few human tumors in which there is a definite occupational etiology In the German dye industry in the early days, when making aniline and other aromatic amines began, it was found that 30 per cent of the cases of carcinoma of the bladder occurred in dye workers

DR TRACY B MALLORY I can find no record of this man's occupation

DR ZAMECNIK I should also like to know whether any x-ray films of the spine and pelvis were taken

DR MALLORY We have x-ray films, but the radiologist says that they are entirely negative and not worth showing

DR ZAMECNIK The primary assumption may be made in this case that the patient died as a result of metastatic carcinoma, and the problem is then reduced to deciding which of several possibilities may be the primary site One may list what seem to be the likelier possibilities—carcinoma of the bladder, the rectosigmoid and the prostate—and discuss them in reverse order

Three symptoms point to disease in the neck hoarseness, dryness of the throat and loss of taste Carcinoma of the larynx accounts for between 1 and 5 per cent of all carcinomas It can explain the hoarseness and all symptoms in the cervical region, but carcinoma of the larynx usually remains localized until late and seldom metastasizes to a great distance It does not appear to be a good possibility when most of the pathologic findings relate to the abdomen

When one is dealing with metastatic carcinoma of the prostate, the acid phosphatase activity is generally elevated and is practically always elevated when there is metastasis to bone This diagnosis has in its favor the fact that carcinoma of the bladder frequently results from extension

of the process from the prostate, indeed, possibly 50 per cent of carcinomas of the bladder are tensions from the prostate Carcinoma of prostate, however, metastasizes to the bone about 70 per cent of the cases Of this 70 per cent, about 85 per cent are osteoblastic and should be associated with a high acid phosphatase level Therefore, although carcinoma of the prostate is a disease that frequently extends through to the bladder, one would not expect such extracapsular prostatic disease to remain dormant On the whole, one may rule out carcinoma of prostate

We should also consider carcinoma of the rectosigmoid Thirty per cent of carcinomas of the gastrointestinal tract are rectal, and of these, two thirds are rectosigmoid I think that it is unlikely that a metastatic carcinoma would localize in the rectosigmoid region and produce an obstruction It is more probable that disease occurred primarily in this region Carcinomas of the rectosigmoid metastasize freely, usually to the inferior mesenteric nodes and frequently, by extension or metastasis, to the liver, lungs and brain I believe that carcinoma of the rectosigmoid cannot be ruled out

The final possibility is carcinoma of the bladder When all cases of carcinoma of the bladder are taken into account, 75 per cent of the patients fail to survive five years Usually, however, when recurrence occurs it does so locally, and metastases are generally not widespread Death most frequently occurs as a result of obstruction of the ureters or infection of the urine and pyelonephritis The aspiration biopsy of the mass in the neck showed "metastatic carcinoma consistent with bladder origin," so that I assume that it was squamous-cell carcinoma On the other hand, an adenocarcinoma was found in the rectosigmoid and I therefore think that it is sound to assume that there were two separate primary neoplastic processes present in this patient One was carcinoma of the bladder, which was discovered five years previously and which was treated with radon implants There may have been some residual tumor in the submucosa, later metastasizing to the cervical region and possibly extending through into the prostate The latter situation is a rather frequent process My second diagnosis is adenocarcinoma of the rectosigmoid, with metastases to the retroperitoneal nodes, the liver and possibly the mediastinum The terminal event may have been due to cholangitis associated with a partially obstructive jaundice, and the effusion in the knee may have been a result of terminal septicemia

DR EDWARD BENEDICT I did the peritoneoscopy on this patient, and I thought that the findings were consistent with biliary cirrhosis I could not see metastatic carcinoma in either the liver or the peritoneum But, of course, peritoneoscopy is

limited, it shows only surface lesions, and a retroperitoneal carcinoma can easily be missed

CLINICAL DIAGNOSES

Carcinoma of bladder
Carcinoma of rectum

DR. ZAMECNIK'S DIAGNOSES

Carcinoma of urinary bladder, with cervical metastasis and probable extension through to prostate
Adenocarcinoma of rectosigmoid, with metastases to retroperitoneal lymph nodes, liver and possibly mediastinum
Terminal cholangitis and septicemia

ANATOMICAL DIAGNOSES

Colloid carcinoma of gall bladder, with widespread metastases.
Epidermoid carcinoma of bladder, with cervical metastases
Adenocarcinoma of rectum
Adenocarcinoma of prostate
Biliary cirrhosis of liver, slight

PATHOLOGICAL DISCUSSION

DR. MALLORY Dr Zamecnik listed three possibilities carcinoma of the bladder, infiltrating adenocarcinoma of the rectum and a probable cancer of the prostate. The patient had all three. The bladder at the time of autopsy showed no evidence of recurrence, but a large lymph node in the neck from which the aspiration biopsy had been taken, when removed at autopsy, showed a poorly differentiated squamous-cell carcinoma entirely consistent with bladder origin and closely resembling a bladder tumor. We also verified the fact that he had carcinoma of the prostate, which was a well differentiated adenocarcinoma resembling in no way the tumor of the bladder, and we could be quite certain that it was a second primary tumor. The tumor of the rectum was also an adenocarcinoma, but once more was well differentiated, slightly polypoid in character, showing slight invasion of the wall, and apparently entirely localized. On the other hand, the retroperitoneal lymph nodes were diffusely and markedly enlarged and, on gross examination, obviously filled with carcinoma.

We also found at autopsy a gall bladder that had a thick, firm, hard wall and a diffuse thickening of the wall of the common bile duct. There was a large stone in the gall bladder, as there usually is in cases of primary carcinoma of the gall bladder. The gall-bladder tumor showed quite marked mucin formation, and the majority of the metastatic lymph nodes showed a frank colloid carcinoma, whereas there was no suggestion of colloid formation in the rectal tumor. Our final opinion on this case was that the patient had four inde-

pendent primary cancers and that it was the cancer of the gall bladder that produced the metastases and resulted in death, and not the other three that were apparent on clinical examination

CASE 32452

PRESENTATION OF CASE

A twenty-seven-year-old crane operator entered the hospital for study of a "rib tumor" discovered during a routine x-ray examination.

For several years the patient had experienced moderate pain in the right shoulder posteriorly that occurred particularly when he remained in the sitting position for any length of time. Occasionally he had to stop playing the piano because of this pain, which never seriously interfered with other activities, however. Four months before entry a routine chest x-ray film taken at his place of employment was found to show a "rib tumor." Review of a similar chest plate taken five years previously disclosed a smaller tumor in the same location. Two weeks before entry, the patient had an attack of "pleurisy" with sharp pain that was aggravated on inspiration and was most marked over the sixth costal rib on the right side. This episode lasted two days but did not interfere with any activity. There had been no cough, fever, chills, night sweats, fatigue, dyspnea, dysuria, flank pain or weight loss.

Physical examination was negative except for markedly impaired hearing in the left ear.

The temperature, pulse and respirations were normal. The blood pressure was 140 systolic, 100 diastolic.

Examination of the blood showed a white-cell count of 10 550 and a hemoglobin of 13.8 gm. The total protein was 7.0 gm, the phosphorus 2.6 mg and the alkaline phosphatase 3.0 Bodansky units per 100 cc. A blood Hinton test was negative.

X-ray examination of the chest revealed localized cystic widening of the posterior medial aspect of the right second rib in the region of the rib angle. X-ray films of the pelvis, arms and hands were normal.

On the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HUGH F. HARE* We have three sets of x-ray films showing the tumor. The first film reveals a lesion involving the second rib. There is only slight expansion of the rib, the lesion appears cystic and involves the cortex, but there is no evidence of any break through the cortex. Approximately 3 cm. of bone was involved at that time. The second film, which was taken five years

*Radiologist, Lahey Clinic

which showed adenocarcinoma (Grade II) Aspiration biopsy of the mass in the neck was reported as showing "metastatic carcinoma consistent with bladder origin" Peritoneoscopy revealed a large blue-gray liver No metastases were seen in the liver or peritoneum Omentum adherent around the gall bladder prevented visualization of that region

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CASE 32452

PRESENTATION OF CASE

A twenty-seven-year-old crane operator entered the hospital for study of a "rib tumor" discovered during a routine x-ray examination.

For several years the patient had experienced moderate pain in the right shoulder posteriorly that occurred particularly when he remained in the sitting position for any length of time. Occasionally he had to stop playing the piano because of this pain, which never seriously interfered with other activities, however. Four months before entry a routine chest x-ray film taken at his place of employment was found to show a "rib tumor." Review of a similar chest plate taken five years previously disclosed a smaller tumor in the same location. Two weeks before entry, the patient had an attack of "pleurisy" with sharp pain that was aggravated on inspiration and was most marked over the sixth costal rib on the right side. This episode lasted two days but did not interfere with any activity. There had been no cough, fever, chills, night sweats, fatigue, dyspnea, dysuria, flank pain or weight loss.

Physical examination was negative except for markedly impaired hearing in the left ear.

The temperature, pulse and respirations were normal. The blood pressure was 140 systolic, 100 diastolic.

Examination of the blood showed a white-cell count of 10,550 and a hemoglobin of 13.8 gm. The total protein was 7.0 gm, the phosphorus 2.6 mg and the alkaline phosphatase 3.0 Bodansky units per 100 cc. A blood Hinton test was negative.

X-ray examination of the chest revealed localized cystic widening of the posterior medial aspect of the right second rib in the region of the rib angle. X-ray films of the pelvis, arms and hands were normal.

On the tenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. HUGH F. HARE* We have three sets of x-ray films showing the tumor. The first film reveals a lesion involving the second rib. There is only slight expansion of the rib, the lesion appears cystic and involves the cortex, but there is no evidence of any break through the cortex. Approximately 3 cm of bone was involved at that time. The second film, which was taken five years

*Radiologist, Labey Clinic

later, shows an increase in the size of the tumor, as well as greater expansion of the rib than at the examination five years previously. In a third film taken a month after the second one, the lesion is practically unchanged, appearing multilocular, cystic and expansile.

The first problem that must be considered, if the diagnosis of rib tumor is correct, is whether the lesion was benign or malignant. A tumor that lasted for five years is quite likely to be benign, and we have sufficient evidence in the normal blood findings, the negative Hinton test and the normal blood protein, phosphorus and alkaline phosphatase that this was a localized process. We have further evidence that it was not malignant in that the lungs were clear. One possibility that should never be overlooked in a bone tumor, however, is a reticulum-cell sarcoma, which is a slowly growing lesion and is present a number of years before symptoms become apparent. I do not believe that we need consider plasmocytoma with a duration of five years, but we must consider an enchondroma or chondroma that may have become malignant. Against malignancy, however, is the fact that in this tumor we cannot see any break through the cortex. Therefore, I think that we can rule out a malignant lesion.

Of the benign lesions we must consider bone tumors and granulomas. I do not believe that we can make a differential diagnosis between granulomas and benign tumors from the x-ray films. The most frequent tumor that is found in this location is the giant-cell tumor. Out of a series of 400 cases described by Copeland and Geschickter* 25 per cent were giant-cell tumors of the rib. Another point in favor of bone tumor is that the patient was in the correct age group, being under thirty. Another possibility is bone cyst. The patient was older than the average patient with bone cyst, and the lesion is usually not multilocular, on the other hand, it was close to the epiphyseal margin, cysts generally occurring in such a location or in the metaphysis of the bone.

Proceeding to the granulomas, we should consider fibrous dysplasia, localized eosinophilic granuloma and ossifying fibroma, all of which can fairly well be included because of the fact that this was a multilocular lesion and had been present for a long time. It would not surprise me to find that this lesion belongs in the group of granulomas, because I have seen similar cases. The next possibility is a neurofibroma or von Recklinghausen tumor that had grown into the rib. These are extremely slowly growing processes. There is certain evidence in the x-ray films that could be so interpreted. The long-standing history, however, and the fact that the lesion was multilocular make me favor a giant-cell tumor.

DR JAMES R. LINGLEY: What about the possibility of localized osteitis fibrosa cystica? Such a lesion is not too infrequent in the ribs. We have had several cases in the younger age group.

DR HARE: I think that that is a good possibility, but I included it when I mentioned fibrous dysplasia. It is just a difference in terminology.

CLINICAL DIAGNOSIS

Benign rib tumor

DR HARE'S DIAGNOSIS

Benign giant-cell tumor

ANATOMICAL DIAGNOSIS

Fibrous dysplasia of rib.

PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: The rib was resected, and a tumorlike expansion was found. On cutting into this it was seen to be filled with solid material, somewhat gritty in character. Microscopic examination showed marked thinning of the cortex. The marrow cavity was filled with connective tissue in which were many trabeculae of rather poorly formed bone—in other words, the characteristic picture of fibrous dysplasia. There was no cystic cavity that we could find, it was therefore not a true bone cyst.

The question comes up how cases of this type should be handled and how radical one should be in the treatment. Fibrous dysplasia is a chronic lesion that rarely if ever heals completely, but once the patient has passed beyond puberty, the extension is slow and usually stops completely. There is no record of a case of fibrous dysplasia that was followed by osteogenic sarcoma or other form of malignant tumor, so that there is no probability of harm to the patient if it is left untreated. When it occurs in the long bones there is the possibility of pathologic fracture. In the rib that is fairly unlikely, and I think that, if there had been any way in which the diagnosis could have been established, there was not much need for operating on this man. His disability was so slight that he was able to go through three years of military service.

Dr Shipman, this was a patient of yours. Do you wish to add anything?

DR THOMAS L. SHIPMAN: There is little that I can add. The second x-ray film was taken at a time when the patient was being re-employed after discharge from the service. The swelling of the rib five years previously had been missed, but I do not believe that we need apologize for that. We did spot the lesion in the rib in the later film and referred him to the hospital for treatment.

*Geschickter, C. F., and Copeland, M. M. *Tumors of Bone* 709 pp. New York: American Journal of Cancer 1931.

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COUNCIL MEETING

A STATED meeting of the Council of the Massachusetts Medical Society was held on October 2, 1946.

On the recommendation of the Committee on Arrangements, the length of the annual meeting in 1947 was extended to cover three instead of the usual two and a half days. In this connection, acting on the recommendation of the Committee on Postwar Planning, the Council directed the Committee on Arrangements to provide for adequate discussion of some topic in medical economics.

Acting also on the recommendation of the Committee on Postwar Planning, the Council authorized the appointment of a special committee to study the medical resources of the Commonwealth, especially regarding how best to mobilize these resources in

time of war or other disaster. This committee will act with a similar committee of the American Medical Association, which will direct its attention to the same subject on the national level.

In connection with the plan to provide medical care for veterans by civilian physicians, the Council agreed to differentiate the specialist and the general practitioner. A communication from the Veterans Bureau indicated that this was necessary if the plan was to go forward. Such a differentiation and the formula by which it will be arrived at were agreed on only for the purposes of the Veterans Administration. The Council likewise agreed that the fee schedule adopted by the Council on April 10, 1946, be reduced by 20 per cent when the services called for in the schedule are rendered by a general practitioner.

Two communications, one from the John Hancock Life Insurance Company and the other from the Liberty Mutual Insurance Company, were referred to the Committee on Public Relations for study by a subcommittee set up for this purpose. These communications dealt with the same subject—the merits of sickness-insurance plans sponsored by old-line insurance companies.

BAL—A CURE FOR HEAVY-METAL POISONING

THE ill wind that blew chlorine gas from the German lines across no man's land in World War I and that started a race for the development of more and deadlier chemicals for use in warfare has now blown in some good. During the present war the search for antidotes to neutralize the action of arsenical vesicants, one of the most potent of which is lewisite, has resulted in the discovery of a therapeutic agent that is effective in counteracting the local and systemic effects of poisoning with arsenicals and with some other heavy metals. The agent is 2,3-mercaptopropanol and has been called BAL (British anti-lewisite). Announcement of the development and properties of this substance has been withheld until recently for reasons of security.

The discovery was made by Peters and his associates at Oxford and was based on earlier American work, which suggested that the toxic action of

arsenic on cells is due to the inactivation of thiol-containing enzymes. A search for other thiol compounds that would compete more effectively for the arsenic resulted in the development of BAL. Many different agencies and groups of workers in Great Britain and in the United States collaborated in these investigations throughout the latter part of the war, and the clinical studies in particular have continued since the close of hostilities. Announcements of the discovery of BAL, together with brief accounts of its pharmacologic and toxicologic properties and of the results of preliminary clinical trials in cases of arsenical and mercurial poisoning, have recently been made.^{1, 2}

Experiments have shown that trivalent arsenicals exert their toxic action by combination with -SH groups of the activating protein of enzyme systems. Tissue respiration is interfered with by the action of the arsenicals on the large group of -SH enzymes essential for carbohydrate transformations and fat metabolism. The enzyme inhibitions produced by lewisite and arsenic can generally be prevented by BAL or by closely related dithiols. Furthermore, even when established, these inhibitions can be reversed by BAL and to a lesser extent by glutathione. In this reversal, BAL exhibits greater affinity for arsenic than do the thiols of the attacked tissue. Certain inhibitions produced by arsine, however, are actually enhanced by BAL, apparently because of the inherent toxicity of BAL itself for the enzyme system attacked by the arsine.

If trypanosomes or spermatozoa are subjected to lethal concentrations of arsenic they lose all motility and show early degenerative changes. If BAL is added, they regain their motility and normal cytologic appearance. The arsenic is actually removed from the damaged cells, as shown by an increase in the arsenic content of the supernatant fluid. BAL was found to be highly effective in the treatment of systemic poisoning in rabbits even when given several hours after the toxic dose of an arsenical.

It was also found that human beings could tolerate effective doses of BAL. Untoward reactions, however, were encountered when larger doses were used. An intramuscular dose of 5 mg per kilogram of BAL in oil may cause a patient some discomfort in

the form of lacrimation, burning of the lips, drying of the mouth and throat, generalized muscular aching, restlessness and nervousness, but no severe reactions were encountered and the effects of smaller doses were minimal. The untoward reactions to BAL seldom persisted for more than thirty minutes, and injections could be repeated at four-hour intervals.

BAL has been used in the treatment of the various arsenical reactions that occur during the course of the treatment of syphilis. These have included arsenical encephalitis, dermatitis, agranulocytosis, fever and jaundice. The early reports indicate a dramatic amelioration of symptoms and a marked reduction in the expected mortality. One interesting feature of BAL therapy in both experimental and clinical arsenic poisoning has been the extremely rapid increase in the excretion of arsenic that follows immediately after the injection of the antidote.

Extensive studies have also been made on the antidotal effects of BAL in experimental mercury poisoning, and the results have been striking. Apparently the interaction of one mol of BAL with one of bivalent mercury in vitro results in the formation of an insoluble compound, but the addition of another mol of BAL produces a substance that is difficult to dissociate but highly soluble. The efficacy of BAL in the treatment of mercurial poisoning is considered to be due to the rapid formation and excretion of the latter.

In the case of both mercurial and arsenical poisoning the efficacy of treatment is greatly decreased the longer it is delayed. Most dogs were protected, however, as long as two or three hours after intravenous injection and five hours after oral administration of mercuric chloride. When treatment was delayed for five hours after ingestion, in most fatal cases death was not associated with renal insufficiency but rather was the result of a severe gastroenteritis, which often was far advanced before the first dose of BAL was administered.

Clinical trials of BAL in human arsenical and mercurial poisoning were reported by Luetscher at the recent meeting of the American Society for Clinical Investigation.³ Dermatitis was the most frequent form of arsenic intoxication and responded

to intunction or injection of BAL. The results in cases of hepatitis and blood dyscrasias were less striking. No deaths occurred in the 30 consecutive cases of arsenical intoxication that were treated with this drug. An increased urinary excretion of arsenic regularly followed the BAL treatment in cases of dermatitis, appearing each time that the course of treatment was repeated. This increase coincided with the appearance of BAL-like material in the urine. In cases of hepatitis, arsenic excretion was not regularly affected by the injections of BAL. Luetscher also reported apparent benefit from large doses of BAL in the treatment of 26 cases of mercurial poisoning. The mortality was about half the previous rate for the Johns Hopkins Hospital. The most striking features of BAL therapy were the prompt relief of even the most alarming symptoms, the rapidity with which the patients made a complete recovery and the low incidence of significant renal complications.

REFERENCES

1. Waters, L. L., and Stock, C. BAL (British anti-lewisite). *Science* 102:601-606, 1945.
2. Gilman, A. Therapeutic applications of chemical warfare agents. *Federation Proc.* 5:292, 1946.
3. These data and others dealing with BAL are contained in a series of eleven papers by several authors appearing in the July, 1946 issue of the *Journal of Clinical Investigation*.

MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

CONRO—Arthur C. Conro, M.D., of Attleboro, died August 18. He was in his seventy-seventh year.

Dr. Conro received his degree from Chattanooga Medical College in 1901. He was a member of the New England Otological and Laryngological Society. His widow and a son survive.

CROSBY—L. Marshall Crosby, M.D., of Wakefield, died October 24. He was in his seventieth year.

Dr. Crosby received his degree from Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, in 1901. He was a former president of the Middlesex East District Medical Society and a fellow of the American Medical Association. His widow survives.

O'DEA—Patrick J. O'Dea, M.D., of Fitchburg, died September 25. He was in his sixtieth year.

Dr. O'Dea received his degree from University of Vermont College of Medicine in 1912.

SULLIVAN—Arthur J. Sullivan, M.D., of Fall River, died August 6. He was in his fifty-seventh year.

Dr. Sullivan received his degree from Jefferson Medical College of Philadelphia in 1912. A brother and a sister survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR SEPTEMBER, 1946

DISEASES	RÉSUMÉ		
	SEPTEMBER 1946	SEPTEMBER 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	99	162	66
Chancroid	1	1	*
Chicken pox	114	90	105
Diphtheria	51	11	10
Dog bite	1078	924	923
Dysentery bacillary	5	11	23
German measles	56	49	30
Gonorrhea	441	405	410
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	0	*
Malaria	21	102	6
Measles	204	145	150
Meningitis meningococcal	5	4	6
Meningitis Pfeiffer bacillus	1	0	0
Meningitis pneumococcal	2	1	2†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	1	0	0†
Meningitis other forms	5	2	1†
Meningitis undetermined	1	5	4†
Mumps	101	194	194
Pneumonia lobar	5	57	106
Salmonella infections	20	9	9
Scarlet fever	135	140	240
Syphilis	52	292	163
Tuberculosis pulmonary	205	205	215
Tuberculosis other forms	20	14	23
Typhoid fever	5	0	3
Undulant fever	1	2	2
Whooping cough	520	570	474

*Made reportable December 1943

†Four year average

COMMENT

Diseases reported at an incidence above the seven-year median included anterior poliomyelitis, chicken pox, diphtheria, German measles, measles, meningococcal meningitis, Salmonella infections and whooping cough.

Diseases reported below the median prevalence included bacillary dysentery, mumps, lobar pneumonia, scarlet fever and undulant fever.

Diphtheria continued to rise for the fifth consecutive month, the incidence being over five times the median prevalence. It is the highest for September in thirteen years.

Although above the median prevalence, poliomyelitis had an incidence of less than two thirds that of last year.

Undulant fever is reported at the lowest in seven years.

Lobar pneumonia has reached an all-time low.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Amherst, 1, Barre, 1, Bellingham, 1, Boston, 9, Chicopee, 1, East Bridgewater, 1, Everett, 2, Falmouth, 1, Gardner, 1, Gloucester, 2, Greenfield, 1, Leverett, 1, Lowell, 2, Lunenburg, 1, Lynn, 2, Malden, 2, Medford, 2, Montague, 1, Natick, 1, Newton, 2, Northampton, 1, North Adams, 7, Northridge, 1, Northfield, 2, Revere, 2, Shelburne, 2, Shrewsbury, 1, Southboro, 1, South Hadley, 1, Springfield, 1, Sudbury, 1, Sutton, 1, Walpole, 3, Waltham, 5, Watertown, 1, Wayland, 1, Webster, 1, Wellesley, 2, Weymouth, 1, Worcester, 29, total, 99.

Diphtheria was reported from Boston, 23, Cambridge, 2, Everett, 1, Hanson, 1, Leominster, 1, Medford, 1, New Bedford, 2, Somerville, 19, Worcester, 1, total, 51.

Dysentery, bacillary, was reported from Boston, 2, Wrentham (State Hospital) 3, total, 5.

Lymphocytic choriomeningitis was reported from Agawam, 1, total, 1.

Malaria was reported from Attleboro, 1, Boston, 4, Brockton, 2, Cambridge, 2, Dedham, 1, Hingham, 1, Lanesboro, 1, Lynn, 1, Newton, 3, Peabody, 1, Quincy, 1, Somerville, 1, Southboro, 1, Springfield, 1, Woburn, 1, Worcester, 1, total, 23.

Meningitis, meningococcal, was reported from Adams, 1, Boston, 1, Chicopee, 1, Fitchburg, 1, Leominster, 1, Lowell, 1, Lynn, 1, Newburyport, 1, total, 8.

Meningitis, Pfeiffer bacillus, was reported from Haverhill, 1, total, 1.

Meningitis, pneumococcal, was reported from Chicopee, 1, Mansfield, 1, total, 2.

Meningitis, streptococcal, was reported from Cambridge, 1, total, 1.

Meningitis, other forms, was reported from Boston, 2, total, 2.

arsenic on cells is due to the inactivation of thiol-containing enzymes. A search for other thiol compounds that would compete more effectively for the arsenic resulted in the development of BAL. Many different agencies and groups of workers in Great Britain and in the United States collaborated in these investigations throughout the latter part of the war, and the clinical studies in particular have continued since the close of hostilities. Announcements of the discovery of BAL, together with brief accounts of its pharmacologic and toxicologic properties and of the results of preliminary clinical trials in cases of arsenical and mercurial poisoning, have recently been made.^{1, 2}

Experiments have shown that trivalent arsenicals exert their toxic action by combination with $-SH$ groups of the activating protein of enzyme systems. Tissue respiration is interfered with by the action of the arsenicals on the large group of $-SH$ enzymes essential for carbohydrate transformations and fat metabolism. The enzyme inhibitions produced by lewisite and arsenic can generally be prevented by BAL or by closely related dithiols. Furthermore, even when established, these inhibitions can be reversed by BAL and to a lesser extent by glutathione. In this reversal, BAL exhibits greater affinity for arsenic than do the thiols of the attacked tissue. Certain inhibitions produced by arsine, however, are actually enhanced by BAL, apparently because of the inherent toxicity of BAL itself for the enzyme system attacked by the arsine.

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THE EFFECT OF ANTICOAGULANTS ON THE PENICILLIN THERAPY AND THE PATHOLOGIC LESION OF SUBACUTE BACTERIAL ENDOCARDITIS*

WALTER S. PRIEST, M.D.,† JACQUES M. SMITH, M.D.,‡ AND CHARLES J. MCGEE, M.D.§

CHICAGO

THE nature of the valvular lesions in subacute bacterial endocarditis makes the use of anticoagulants appear a logical procedure in the prevention of fibrin formation. Such agents should thereby keep the vegetative process at a minimum and theoretically render the bacteria more accessible to antibacterial agents. Also, in theory, the frequency of embolism should be reduced.

Following the isolation of heparin and the demonstration of its ability to prolong the coagulation time of blood, many workers used this substance alone or in combination with chemotherapeutic and other agents in the treatment of subacute bacterial endocarditis. The results of these efforts are summed up by McLean et al.,¹ Lichtman,² Katz and Elek,³ and Hines and Kessler.⁴ From his own experience and that of others, Katz concluded that the use of heparin in subacute bacterial endocarditis should be abandoned. Leach and his co-workers⁵ were unable to find at autopsy any significant effect of either heparin or the sulfonamides on the valvular lesions; in addition, the vegetations were swarming with organisms.

Because of the reports of McLean and Leach, the use of anticoagulants was not considered in June, 1943, when our studies on the effect of what were then regarded as large doses of penicillin on subacute bacterial endocarditis were begun. But Loewe,⁶ who at the same time was studying the effect of similar penicillin dosage (200,000 units a day), was also using heparin, administered intramuscularly in Pitkin menstuum, and considered it essential to success. This opinion was maintained in a subsequent paper.⁷ In December, 1943, Dr. Loewe kindly supplied us with sufficient heparin in Pitkin menstuum for a small series of patients. It was our

purpose to treat an equal number of patients with and without anticoagulants, such as heparin and dicumarol,^{||} and also to determine the relative efficacy of the compounds.

EFFECT ON EFFICACY OF PENICILLIN

To date, we have employed penicillin in 37 cases of subacute bacterial endocarditis, in all but 2 of which administration was by continuous intravenous drip. The clinical results in the first 34 cases, which furnished the material analyzed in this report, were reported elsewhere.⁸ Eight patients received heparin alone, 3 received dicumarol alone, 4 received heparin and dicumarol and 19 were treated without anticoagulants.

When heparin and dicumarol were used in the same patient, one drug was used during half the course of penicillin therapy and the other during the remainder, or one was used during a full course and the other during a subsequent course.

In treating the patient in Case 1, it was found that digitals partially or completely nullified the effect of heparin. Hence, in subsequent patients, dicumarol was used whenever digitalization became necessary. The pertinent data concerning the patients receiving anticoagulants are summarized in Table 1.

In Cases 1, 3, 4, 5, 6, 7, 8 and 20, all or part of the heparin was administered subcutaneously or intramuscularly in Pitkin menstuum. Whether given subcutaneously or intramuscularly or even in combination with local anesthetics, this material proved so painful that all but 2 of the patients receiving it refused to continue the treatment. Liquid heparin** was therefore added to the penicillin saline intravenous mixture. Determinations of the coagulation time by the Lee-White modification of Howell's method were made daily and frequently twice daily, except in Case 6, in which the capillary method was used. An attempt was made to maintain the coagulation time between 30 and 60 minutes, as recom-

*From the Department of Medicine, Wesley Memorial Hospital, Northwestern University.

†The penicillin used in this study was furnished by Commercial Solvents Corporation, Terre Haute, Indiana; Schenley Laboratories, Incorporated, Lawrenceburg, Indiana; Lederle Laboratories, Incorporated, New York City; and the National Research Council.

‡Associate in Medicine, Northwestern University; attending physician, Wesley Memorial Hospital.

§Formerly resident in Medicine, Wesley Memorial Hospital.

||Fellow in Medicine, Northwestern University.

| Supplied through courtesy of Abbott Laboratories, Incorporated, North Chicago.

**The liquid heparin was furnished partly by Abbott Laboratories, Incorporated, North Chicago, and partly by Hoffmann-La Roche, Incorporated, Nutley, New Jersey.

Meningitis undetermined, was reported from Revere, 1, total, 1

Salmonella infections were reported from Boston, 1, Brewster, 1, Brockton, 4, Holyoke, 1, Lynn, 1, Methuen, 3, Newton, 1, Northfield, 3, Salem, 1, Swampscott, 1, Topsfield, 1, Watertown, 1, Worcester, 1, total, 20

Septic sore throat was reported from Boston, 2, Lynn, 1, Williamstown, 2, total, 5

Tetanus was reported from Duxbury, 1, total, 1

Trichinosis was reported from Boston, 1, total, 1

Typhoid fever was reported from Boston, 1, Chelsea, 1, Holyoke, 1, total, 3

Typhus fever was reported from Boston, 1, total, 1

Undulant fever was reported from New Bedford, 1, total, 1

MISCELLANY

CAMPAIGN TO COMBAT HEART DISEASE

The initiation of a nationwide program of public education and information on diseases of the heart was recently announced by officials of the American Heart Association, Incorporated

The program, according to Dr Howard F West, of Los Angeles, president of the association, will have as its prime purpose "the dissemination of educational information to the public in a broad effort to retard the rapid increase of heart disease throughout the nation"

"Fatalities ascribed to diseases of the heart," Dr West said, "are greater than the total of the next five leading causes of death. It is essential, therefore, that the public know more about the significance of blood pressure, infections, obesity, rheumatic fever and other factors which contribute to various types of heart disease"

It is estimated that there are more than 4,000,000 people in the United States today who have heart disease. Diseases of the heart and blood vessels, including cerebral hemorrhage, accounted for 575,000 deaths in 1944. Fatalities from the five other leading causes in 1944 were as follows: cancer, 171,000, accidental deaths, 95,000, nephritis, 92,000, pneumonia, 64,000, and tuberculosis, 55,000. In addition to accounting for more fatalities than these five causes combined, heart disease is responsible for an annual loss of more than 100,000,000 work days.

Officials of the American Heart Association state that the association's program will call for emphasis on educational work with schools, parent-teacher associations and other groups concerned with children because of the importance of rheumatic fever and heart disease. According to recent surveys, this scourge of children causes more than five times as many deaths as the combined total of deaths from infantile paralysis, scarlet fever, diphtheria, measles, meningitis and whooping cough. It is a serious disease among adults, too, as illustrated by the estimated 40,000 veterans who acquired the disease during their recent military service.

The war forcibly dramatized the need for a national health program designed to retard the increase in heart disease cases. An estimated 10 per cent of the men rejected by Selective Service were disqualified because of cardiovascular diseases. In a survey of a special sampling of 5000 rejectees for cardiovascular diseases in five major cities, — Chicago, New York, Boston, Philadelphia and San Francisco, — 50 per cent had been disqualified because of rheumatic heart disease. The second greatest cause of rejection due to cardiovascular diseases was hypertension, which accounted for nearly 26 per cent of the disqualifications.

The educational campaign of the American Heart Association will reach its climax during National Heart Week, to begin on February 9, 1947, which includes St Valentine's Day. It is expected that all branches of medicine, pharmacy, insurance, industry and many other groups interested in health and public welfare will co-operate fully.

Supporting groups will include the following national organizations, which comprise the American Council on Rheumatic Fever of the American Heart Association, American Academy of Pediatrics, American Association of Medical Social Workers, American College of Physicians, American Hospital Association, American Medical Association, American Nurses Association, American Public Health Association, American Rheumatism Association, American School Health Association, National Organization for Public Health Nursing

and National Society for Crippled Children and Adults. The collaboration of the United States Public Health Service, National Tuberculosis Association and others is expected.

NOTICES

ANNOUNCEMENTS

Dr Joseph Factor announces the removal of his office to 475 Commonwealth Avenue, Boston

Dr James S Mansfield, having returned from military service, is resuming the practice of internal medicine at 12 Bay State Road, Boston

BOSTON GASTROENTEROLOGICAL SOCIETY

The next meeting of the Boston Gastroenterological Society will be held in the New Cheever Amphitheater, Dowling Building, Boston City Hospital, on Wednesday, November 13, at 12 noon. Dr Frank H Lahey will speak on the subject "The Management of Biliary-Tract Disease."

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Hotel Beaconsfield on Friday, November 15. The x-ray conference at 4:30 p.m. will be devoted to therapy of benign lesions. At 8:00 p.m., Dr Maurice Lenz will speak on the subject "Cancer of the Breast."

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 19, at twelve noon. Dr Norman H Boyer will speak on the subject "Some Clinical Aspects of Coronary Artery Disease." Dr Samuel Grossman will preside.

Physicians are cordially invited to attend.

AMERICAN MEDICAL ASSOCIATION

At the Centennial Session of the American Medical Association, to be held in Atlantic City, June 9 to 13, 1947, the Scientific Exhibit will include both the history of medicine during the past century and the latest developments of medical science.

Application blanks for space are now available. All applicants must fill out the regular form. Applications close on January 13, 1947, after which time the Committee on Scientific Exhibit will make its decision and notify the applicants.

Application blanks for space should be procured as soon as possible. They are available from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, NOVEMBER 14

FRIDAY, NOVEMBER 15			
*9:00-10:00 a.m.	Carcinoma in situ	Dr Tracy B Mallory	Joseph H Pratt Diagnostic Hospital
*10:00 a.m.-12:00 m.	Medical Staff Rounds	Peter Bent Brigham Hospital	
MONDAY, NOVEMBER 18			
*12:15-1:15 p.m.	Clinicopathological Conference	Peter Bent Brigham Hospital	
TUESDAY, NOVEMBER 19			
*12:15-1:15 p.m.	Clinicoroentgenological Conference	Peter Bent Brigham Hospital	
WEDNESDAY, NOVEMBER 20			
*9:00-10:00 a.m.	Certain Peculiarities of Brain Metabolism	Dr David Rapport	Joseph H Pratt Diagnostic Hospital
*10:30-11:30 a.m.	Medical Clinic	Isolation Building Amphitheater, Children's Hospital	
*12:00 m.	Clinicopathological Conference (Children's Hospital)	Amphitheater, Peter Bent Brigham Hospital	
*2:00-3:00 p.m.	Combined Clinic by the Medical, Surgical and Orthopedic Services	Amphitheater, Children's Hospital	

*Open to the medical profession

(Notices continued on page xiv)

mended by Loewe, and it was found somewhat easier to hold it to these limits when liquid heparin was added to the penicillin solution

By either method of administration there was considerable individual variation in response. In Case 1 the administration of 300 and 200 mg of heparin subcutaneously on succeeding days resulted in a coagulation time of 20 minutes. The injection of 300 mg on each of two further days produced a coagulation time of 55 minutes, and no subsequent daily dose could prevent fluctuations from 10 to 75 minutes. Doses of both 200 and 300 mg a day for periods of three and four days resulted in the same wide variation.

In Case 21 daily doses of 300 mg for eleven days failed to raise the coagulation time above 18 minutes. In Case 3 alternate daily doses of 200 and 100 mg, given in the penicillin solution, maintained a range of 25 to 35 minutes for eight days, after which the same difficulty was experienced. Later, a daily dose of 150 mg was found satisfactory.

In Case 4 two consecutive daily doses of 100 mg in the penicillin solution gave a coagulation time of 50 minutes. After six days heparin was stopped, and for eight days thereafter the range was 20 to 45 minutes. Resumption of 100 mg a day did not change this finding until a dose of 100 mg was given subcutaneously, resulting in a coagulation time of 65 minutes.

In Case 5 a daily dose of 100 mg in the penicillin solution for twenty-eight days resulted in fluctuations between 30 and 55 minutes, with two readings of 65 minutes. Subsequently 200 mg subcutaneously every other day produced a range of 20 to 38 minutes.

In Case 6 the addition of 100 mg to the penicillin solution produced a capillary coagulation time of 14 minutes, comparable to a venous time of 46 minutes. A reduction of the dosage to 50 mg a day produced a range comparable to 13 to 20 minutes for the first three days. Four days later the range increased to 20 to 25 minutes. Thereafter, a subcutaneous injection of 150 mg daily maintained this range for four days, followed by fluctuations from 20 to 40 minutes. The administration of 200 mg a day by the same route did not alter this range.

In Case 7, as well as in others, a cumulative effect, impossible to foresee, was observed. The addition of 200 mg a day to the penicillin solution produced a range of from 10 to 40 minutes. On the fourth day (without heparin) the time was 65 minutes. Two days later a single dose of 200 mg produced a time of 55 minutes, and thereafter, 100 mg a day held it between 30 and 40 minutes.

In Case 8 the administration of 100 mg daily in the penicillin solution held the coagulation time steadily at 30 minutes, 200 and 100 mg, given subcutaneously on alternate days, produced a range of 20 to 30 minutes. During a subsequent course, 175 mg daily in the penicillin solution produced rapid

fluctuations from 20 to 90 minutes for ten days, after which, without alteration of the dose, the coagulation time remained steady between 40 and 50 minutes.

In Case 9 the addition of 200 mg daily to the penicillin solution was required to produce a range of 20 to 55 minutes, fluctuations between two daily determinations being from 20 to 30 minutes.

When dicumarol was used, an attempt was made to maintain the prothrombin time at 260 to 300 per cent of normal. Daily determinations were made. It was even more difficult to adjust the dose of dicumarol to maintain the desired prothrombin time than to adjust the dose of heparin to maintain the desired coagulation time. As with heparin, considerable variation was found in the individual response to dicumarol. In Case 21 a single dose of 300 mg of dicumarol developed a prothrombin time 2000 per cent of normal, the same patient had failed to obtain the desired response from heparin, even with daily doses of 200 to 400 mg for thirty-three days.

A lag of approximately five days from the initial dose of dicumarol to its full effect was observed in nearly every case. Unless this fact is recognized, the prothrombin time for the first few days may lead to overdose. An initial reduced daily course of 300, 200, 100 and 50 mg respectively for the first four days, followed by 50 mg a day, was finally found likeliest to produce and maintain the desired effect.

The duration of the disease before penicillin therapy combined with anticoagulants ranged from one and a half to fifty-two weeks. In 9 cases this was the initial course of therapy. Of the 15 patients receiving anticoagulants, 8 died, it is only fair to say that 2 patients (Cases 19 and 20) were in extremis when admitted. The duration of the disease before penicillin therapy in patients who did not receive anticoagulants ranged from six to forty-two weeks. Of these 19 patients 3 died with active lesions, 1 died of congestive failure, but was shown histologically to have been cured.

The sensitivity of the causative organism to penicillin in vitro ranged from 0.02 to 1.0 units per cubic centimeter in patients receiving anticoagulants, and from 0.02 to 6.0 units in those who did not. Thus the duration of the disease and the sensitivity of the organism to penicillin covered a wide range in both groups.

EFFECT ON EMBOLISM

When the incidence of major embolic phenomena before and during administration of anticoagulants was analyzed, embolism was found to have occurred before but not during administration in 3 cases, both before and during administration in 3, not before but during administration in 2, and neither before nor during administration in 11. Several patients had more than one course of treatment, permitting multiple observations. Thus, whereas anti-

TABLE 1 Data in Patients with Subacute Bacterial Endocarditis Treated with Anticoagulants in Addition to Penicillin

CASE No.	ORGANISM	Penicillin sensitivity in vitro	DURATION OF DISEASE BEFORE PENICILLIN THERAPY, wk	DURATION OF DISEASE AFTER PENICILLIN THERAPY, wk	DURATION OF DISEASE BEFORE COAGULANT THERAPY, wk	DAILY DOSE OF PENICILLIN, units	DAILY DOSE OF ANTICOAGULANT, mg	DURATION OF ANTICOAGULANT THERAPY, days	COAGULATION TIME, min	PROTHROMBIN TIME, % of normal	VASCULAR ACCIDENTS WITHOUT ANTICOAGULANT	VASCULAR ACCIDENTS WITH ANTICOAGULANT	END RESULT	REMARKS
Patients treated with heparin:														
1	<i>Sir viridans</i>	0.02	29	52	52	150,000-200,000	200-300	60	10-75	19	Multiple emboli	Bowel hemorrhage	Death	Autopsy disclosed fibrin-covered tags with embedded bacteria
3	<i>Sir viridans</i>	0.06	7	7	7	200,000	150-200	28	20-70	71	—	—	Recovery	—
4	<i>Sir haemolyticus</i>	0.04	7	7	7	200,000	100	27	20-60	27	—	—	Recovery	—
5	<i>Sir viridans</i>	0.1	8	8	8	200,000	100	27	20-65	40	Cerebral embolism	—	Recovery	—
6	<i>Sir viridans</i>	0.02	27	27	27	200,000	50-200	14	20-45	23	—	—	Recovery	—
18	<i>Sir viridans</i>	0.04	1 1/2	1 1/2	1 1/2	500,000	100-300	33	4-14	18	Embolism in viscera and lungs	Embolism in lungs	Death	Autopsy disclosed large, fresh vegetations on the aortic valve and two fresh vegetations on the pulmonary artery, all filled with bacteria
19	<i>Sir viridans</i>	1.0	4	41	41	500,000	300	51	20-65	9	—	—	Recovery	—
20	<i>Staph aureus</i>	—	4	30	30	500,000	300	10	30-45	8	—	—	Death	—
Patients treated with heparin and dicumarol:														
7	<i>Sir viridans</i>	0.04	30	30	30	500,000	300	11	20-65	60	Cerebral embolism	Multiple embolism	Death	—
8	<i>Sir viridans</i>	0.04	16	16	16	200,000	100-200 (heparin) 100-200 (dicumarol)	29	20-65	29	Cerebral embolism	Multiple embolism	Death	Autopsy disclosed fibrin-covered remnants of fibrin-covered vegetation on the mitral valve, ulceration of the left auricular wall, with fibrin and bacteria
9	<i>Sir viridans</i>	0.08	9	9	9	200,000	250 (heparin) 75-300 (dicumarol)	26	10-30	31	—	—	Recovery	This case was complicated by a relapse after eighteen weeks of therapy
21	Atypical <i>Sir viridans</i>	0.8*	4	17	17	200,000	150-200 (heparin) 100-200 (dicumarol)	27	40-90	26	—	—	Recovery	—
Patients treated with dicumarol:														
10	<i>Sir viridans</i>	0.06	8	8	8	200,000	150-400 (heparin) 41 100 (dicumarol)	39	20-58	29	Cerebral embolism	Cerebral embolism	Death	Autopsy disclosed fibrin-covered, fibrous remnants of mitral-valve vegetations filled with bacteria, as well as a tricuspid ulcer
16	<i>Staph albus</i>	—	1 1/2	11 1/2	11 1/2	400,000	0-200	28	4-17	57	—	Embolism	Death	Autopsy disclosed a stenosed aortic valve, with multiple myocardial papillary hemorrhages and fibrinous pericarditis
13	<i>Sir salicarius</i>	0.04	12	32	32	100,000-400,000	0-200	64	135-750	56	—	—	Recovery	—
						150,000-2,000,000	200-100	273	168-1078	11	Cerebral embolism	Cerebral embolism	Recovery	—

*Organism also sensitive to 0.1 unit per cubic centimeter of streptomycin

EFFECT ON RECOVERY

Without regard for any other factors, 4 patients receiving heparin recovered and 4 died. Of the 3

The most significant factor in recovery is not the use of anticoagulants but the daily penicillin dosage. An analysis of the 34 cases in relation to the daily



FIGURE 3 Case 9

The photograph on the left shows the fibrin-covered remnants (A) of the lesion on the mitral valve. The photomicrograph in the middle shows bacteria (A) entwined in fresh fibrin and platelet thrombi (B) attached to the surface of the fibrin, and that on the right, regenerated endocardium (A) overlying organized fibrin (B), as well as bacteria (C) in the mid-portion of the valve with a more densely organized, and apparently older, layer of fibrin (D) beneath.

patients receiving dicumarol alone, 2 recovered and 1 died. Of the 4 who received combinations of heparin and dicumarol, 1 recovered and 3 died. Of 19 patients receiving no anticoagulants, 14 recovered,

penicillin dosage, revealed that with daily dosages of less than 400,000 units combined with anticoagulants 6 patients died and 2 recovered — a ratio of 3:1. With dosages of 400,000 units or over in addi-



FIGURE 4 Case 13

The photograph on the left shows the fibrin-covered fibrous remnant (A) of the mitral valve. The photomicrograph on the right shows bacteria (A) entwined in fibrin overlying calcium.

ered, of the 5 who died, 4 were found at autopsy to have healing but still active lesions, and 1 (Case 12) who died of congestive heart failure was clinically and histologically cured.

tion to anticoagulants, 1 patient died and 5 recovered — a ratio of 1:5. With dosages of 400,000 units or over without anticoagulants, 4 died and 16 recovered — a ratio of 1:4, these cases included

coagulants may have prevented embolism in 3 cases, in 5 they certainly did not

In 2 additional patients (Cases 1 and 13) massive terminal hemorrhage occurred while anticoagulants

produce a cure, therapy with 1,000,000 units a day, in addition to dicumarol, was started. On the third day massive fatal cerebellar hemorrhage occurred. At autopsy the left cerebellar hemisphere was found

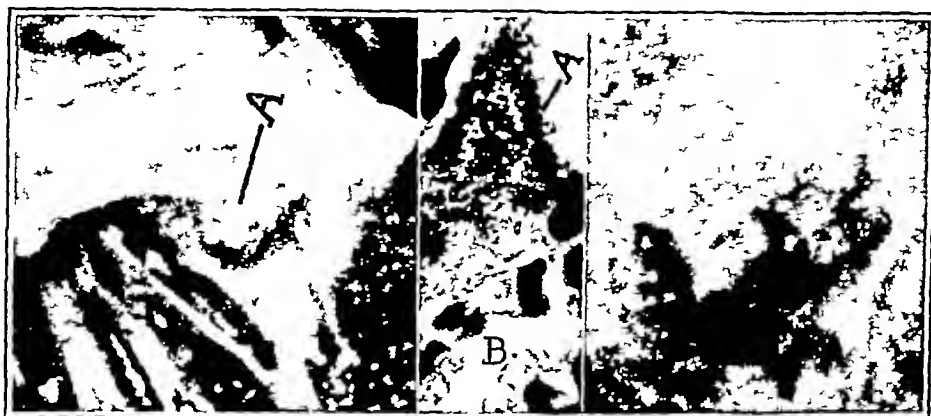


FIGURE 1 Cases 1 and 2

The photograph on the left shows the fibrin-covered fibrous remnants of vegetations of the mitral valve (A) in Case 1, and that on the right, the same in Case 2. The photomicrograph in the middle is of the lesion in Case 1, showing bacteria (A) enmeshed in fresh fibrin and a polymorphonuclear reaction (B) in the adjacent fibrin undergoing organization.

were being given. In Case 1 heparin was being used, in Case 13 no anticoagulants were given during eight months of almost continuous penicillin therapy, during which no hemorrhages occurred and only one

to be destroyed, but the valve showed no friable vegetations (see Fig 4). The valve lesion in Case 1 was similar (see Fig 1). Such accidents cannot be dogmatically evaluated in a disease of this nature,



FIGURE 2 Case 6

The photograph on the left shows fresh polypoid vegetations (A) at the root of the pulmonary artery, and that in the middle, fresh cauliflower-like vegetation (A) of the aortic valve. The photomicrograph on the right is of the latter lesion, showing an abundance of fresh fibrin containing myriads of bacteria (A) overlying organizing fibrin (B).

infarction (in the kidney) was observed. After twenty-four days of 1,000,000 and thirty-eight days of 2,000,000 daily units of penicillin had failed to

but the fact remains that these massive hemorrhages did not occur in any of the patients who did not receive anticoagulants.

In Case 12, one of the longest (forty-two weeks) in point of duration of the disease before penicillin therapy, healing of the vegetations took place without the use of anticoagulants. Only a few micro-

organisms remained at the time of the terminal septicemia, it cannot positively be said that the fibrin present at autopsy was not the result of the superimposed staphylococcal invasion. Somewhat comparable



FIGURE 6 Case 17

The photograph on the left shows the fibrin-covered remnants (A) of the lesion on the mitral valve. The photomicrograph on the right shows cocci (A) enmeshed in fibrin, with underlying organizing fibrin and granulation tissue (B).

sclerotic layers of organizing fibrin were found, and no bacteria were present (Fig. 5).

In Case 17, in which the disease lasted twenty-five weeks before penicillin therapy was instituted, death occurred from secondary staphylococcal septicemia

was Case 7, in which the duration of the endocarditis before penicillin therapy was thirty weeks and in which heparin was given for seventeen days and dicumarol for seventeen days because digitalization was necessary, during a



FIGURE 7 Case 7

The photograph on the left shows fibrous pedunculated remnants (A) of the lesion of the mitral valve, which are covered with small patches of fibrin; there is an ulcerative lesion of the auricular wall (B), which also shows scattered areas of fibrin. The photomicrograph on the right shows bacteria (A) enmeshed in fresh fibrin on the surface of the valvular lesion and underlying fibrin (B) in an advanced stage of organization.

No anticoagulants had been used during treatment of the endocarditis. The remnants of the vegetation were small (Fig. 6), and although we believed there was clinical evidence that some fibrin re-

second course of penicillin, dicumarol was given for twenty days. Grossly and microscopically the lesions (Fig. 7) were similar to those in Case 17.

that of the patient (Case 13) described above in whom massive cerebellar hemorrhage occurred. If this case, which is difficult to classify, is omitted the ratio of deaths to recoveries in patients receiving 400,000 units or more daily without the use of anticoagulants is again about 1:5. Ten of the 16 patients who recovered ultimately received from 1,000,000 to 2,000,000 units a day. In 5 cases of recovery with anticoagulants and 400,000 units or over and in 3 of similar dosage without anticoagulants, smaller daily doses had not resulted in cure. Hence, regardless of anticoagulants, the turning point in favor of recovery was the increase in the daily dose of penicillin to 400,000 units or more. Excluding Case 13, because of the fatal cerebellar hemorrhage, there were only 2 deaths in 12 patients receiving 1,000,000 units or more of penicillin a day. One of these patients (Case 21) received anticoagulants, and the

of death and a coagulation time ranging from 10 to 75 minutes had been maintained for nineteen days previously. During the preceding six months penicillin totaling 15,700,000 units had been given. The patient in Case 2 received no anticoagulants. The involved valve of the heart in both cases showed fibrous tags of vegetations covered by a layer of fresh fibrin (Fig 1). In Case 1 bacteria were present in the fibrin and deeper structures, in Case 2 no microscopic sections were made.

Case 6, in which the duration of the disease before penicillin-heparin therapy was almost identical with that of Case 1, had the largest, most typically cauliflower-like and friable vegetations of any of the autopsied patients (Fig 2). Bacteria in large numbers were found in the fibrin, the outer layer of which was fresh. Yet this patient received heparin in daily doses of 50 to 200 mg during twenty-three of the



FIGURE 5 Case 12

The photograph on the right shows a grossly healed mitral valve, with no visible fibrin. The photomicrograph on the right shows one of the few scattered areas of fibrin (A) overlying the almost completely healed valvular lesion, there is a proliferating endocardial cell (B) in the process of covering over the minute area of fibrin.

other did not. The offending organism in the former was an atypical form of *Streptococcus viridans* that was relatively insensitive to penicillin (0.8 unit per cubic centimeter) but sensitive to streptomycin (0.1 unit per cubic centimeter), which could not be obtained until late in the course of the disease. Continuously negative blood cultures could not be obtained, and embolic phenomena continued until streptomycin proved to be the effective antibacterial agent.⁹ This experience is in line with that of most investigators regarding the combined use of sulfonamides and anticoagulants—namely, that anticoagulants are of no avail if the antibacterial agent is ineffective.²⁻⁵

EFFECT ON PATHOLOGIC LESION

Histologically, no conclusive evidence in favor of the use of anticoagulants could be demonstrated. Grossly, Cases 1 and 2 were comparable. In the former the patient was receiving heparin at the time

twenty-five days of penicillin therapy and was heparinized at the time of death.

The disease in Cases 9 and 13 was of about equal duration at the beginning of penicillin therapy (nine and twelve weeks, respectively). The patient in Case 9 received heparin for twelve and dicumarol for seventeen days of the first course of treatment, and dicumarol for nine days of the second course. In Case 13, with a treatment period of eight months, no anticoagulants were administered except during the terminal five days. Grossly and microscopically the lesions were similar (Figs 3 and 4), but if anything there was less fibrin in Case 13. In Case 9 bacteria were present not only in the fresh fibrin covering the remnants of the vegetations but also in the organized and organizing fibrous tissue of the midportion of the valve, three superimposed layers of fibrin, in varying stages of organization and with bacteria between each layer, were present in one of the valve sections, suggesting that heparin during the first course of penicillin did not prevent fibrin formation.

FOREIGN BODIES IN THE RESPIRATORY TRACT*

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BOSTON

WHEN the diagnosis of foreign body in the respiratory tract has been established by history, physical examination and x-ray study, the surgeon is presented with a problem whose successful solution consists, of course, in the extraction of the foreign body without harm or damage to the patient. Usually, it is the general practitioner who first sees such a patient, and thus the family physician has the first opportunity to make or to miss the diagnosis. Certain pitfalls must be avoided to prevent diagnostic error and improper attempts at removal. This paper briefly reviews some of the salient features of foreign bodies in the various parts of the respiratory tract.

A foreign body in the nose is rare. It is usually self-inserted, and not infrequently the act is concealed by a child. Unilateral nasal discharge in children means that the presence of a foreign body must be ruled out before other possibilities are considered. Within twelve hours after the lodgment of a foreign body in one side of the nose, the secretion becomes purulent. As the days go on, a fetid odor may develop, and over the months and years a rhinolith may form. Bloody nasal discharge occurs immediately after insertion only when the foreign body is sharp and rough. Foreign bodies in the nose are easily seen if looked for. To remove a nasal foreign body, forceps, which often push the foreign body back into the nasopharynx, should not be used; instead, an L-shaped instrument should be employed. If one can get behind a foreign body and pull it forward, it can be readily removed. Cocainization of the nose makes the procedure painless, and adrenalin provides more space by shrinking the turbinates; general anesthesia is seldom necessary. Unless the patient can be absolutely controlled, however, primary general anesthesia is required. The nasopharynx should be guarded, to avoid pushing the object back to be aspirated. Irrigation of the nose often causes ear infection and fails to dislodge the foreign body.

Foreign bodies in the nasopharynx are also infrequent. The patient must cough or gag to drive the foreign body up behind the uvula into the nasopharynx. The symptoms are pain and discomfort referred to the ears, to the back of the head or neck, sometimes to the laryngeal region and sometimes to the cheeks. In other words, unless the nasopharynx can be visualized with a nasopharyngeal mirror, it is unwise to decide that it does not contain a

foreign body. X-ray films demonstrate opaque foreign bodies, such as coins, bones and tacks, but do not show pieces of fruit, nuts or wood. Palpation with the finger is an unsatisfactory method of removal. It should be remembered that if the patient is sitting up, dislodgment of the foreign body may cause it to be lost into the trachea or esophagus or to be pushed forward into the nose. In co-operative adults local anesthesia is quite satisfactory, in children general anesthesia is preferable. The head should be kept low during the operation, and any physician who inspects the results of his adenoidectomies can remove a foreign body from the nasopharynx.

The pharynx and hypopharynx are the most frequent sites for foreign bodies. Ingestion is usually accidental. Because of inability to use the laryngeal mirror, foreign bodies in the hypopharynx are often missed. When the patient complains of pain each time he swallows, a foreign body is present. When there is general soreness that is not made worse by swallowing, the patient has usually suffered only a scratch or abrasion, if the patient gargles a dilute solution of cocaine or pontocaine, the scratch becomes anesthetized and the soreness disappears, but a foreign body such as a bone continues to cause pain on swallowing. This is a simple way to distinguish between an abrasion of the pharynx or hypopharynx and the actual presence of a foreign body. Unless the hypopharynx is carefully inspected with the laryngeal mirror, a foreign body may not be found. The roentgenologist has difficulty in seeing small fishbones imbedded in the base of the tongue or at the bottom of the tonsillar fossa; these are clearly visible with the laryngeal mirror. Once a foreign body has been seen in the pharynx or hypopharynx, hasty grasping must be avoided, since a fumble means its loss. Often, three hands are required for a successful extraction, — one hand for the patient's tongue, one for the laryngeal mirror and one for the forceps used to grasp the bone, — and sometimes an additional pair of hands is needed to hold the patient's head. An example is afforded by a case in which an attempt to grasp, by means of a tongue depressor and a hemostat, a pin visible in the pharynx caused the pin to land in the tracheo-bronchial tree, where, of course, the problem was much more difficult than the one presented by the pin at its original site. In another case, which emphasizes the fact that more harm than good can be done by working under adverse circumstances, a sixteen-month-old baby was seen by its mother to cough and choke after having placed something in its mouth. A physician who examined the child be-

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 21, 1946.

†Instructor in laryngology, Harvard Medical School; assistant surgeon in otolaryngology, Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary; surgeon in otolaryngology, Newton-Wellesley Hospital.

SUMMARY AND CONCLUSIONS

Thirty-four consecutive and unselected cases of subacute bacterial endocarditis treated with penicillin constitute the material for this report. Twelve patients received anticoagulants from the outset of penicillin therapy and also during subsequent courses when more than one course of treatment was given. Two, who were admitted in advanced stages of congestive cardiac failure after varying periods of penicillin therapy without anticoagulants, died after combined penicillin and heparin therapy lasting nine and eight days respectively. One, previously treated for eight months without anticoagulants, suffered massive cerebellar hemorrhage three days after a course of penicillin combined with dicumarol had been begun. Nineteen patients were treated without anticoagulants at any time.

Death occurred in 12 cases in the entire series, and autopsy was performed in 10. There were 4 deaths among the patients who received anticoagulants from the outset of therapy, and 4 among those who received anticoagulants twelve, nine, eight and five days, respectively, at the end of long periods of penicillin therapy. There were 4 fatal cases in which no anticoagulants were given. In 1 of these the patient was histologically cured but died of congestive heart failure. The ratio of deaths to recoveries in patients receiving less than 400,000 units of penicillin—all of whom received anticoagulants at some time—was 3:1. The ratio in patients daily receiving 400,000 units or more of penicillin was 2:5 when anticoagulants were used throughout or during part of the therapy, whereas on a similar schedule, the ratio was 1:5 in patients treated without anticoagulants at any time.

In 5 cases anticoagulants failed to prevent major embolism, in 3 prevention was possibly obtained by this means, and in 11 no major embolic phenomena were observed before or during the use of anticoagulants. Of the 19 patients treated without anticoagulants at any time, 6 had major embolism and 13 did not.

We could find no way of determining whether anticoagulants prevented further clotting at the site of embolism.¹⁰

Gross and microscopic specimens from patients treated with and without anticoagulants are presented. The most typically polypoid and cauliflower vegetations were found in a patient who died at the end of twenty-five days of combined penicillin and heparin therapy. An abundance of fresh fibrin was present on the vegetations. The most nearly complete stage of healing was present in a patient who did not receive anticoagulants. All other lesions showed advanced stages of healing, and yet all showed some fresh fibrin on the surface. The amount

of fresh fibrin present on the lesions in patients treated with anticoagulants was not demonstrably less than that on the lesions in untreated patients.

Generally speaking, thrombosis at the site of the intravenous needle was less in the patients receiving heparin incorporated in the penicillin saline mixture. Small amounts of heparin (50 mg) added to the mixture when the preferable intravenous drip method of administration is used, may aid in retarding venous thrombosis.

Since considerable variation in response to the same dose of heparin or dicumarol was found in the same and in different patients, no standardization of dosage was possible.

No statistical, anatomic or histologic evidence could be found that anticoagulants are a necessary adjunct to penicillin therapy of subacute bacterial endocarditis.

If the daily dose of penicillin is adequate and treatment is continued long enough, healing of the vegetations will take place as well without as with anticoagulants. The rate of recovery was 100 per cent in our latest 15 consecutive cases, in most of which the patients daily received 1,000,000 units or more. All these patients were treated without the use of anticoagulants.

It is doubtful that anticoagulants prevent major embolism.

Fatal hemorrhage resulting from the use of anticoagulants was suggested, although not proved, in 2 of the cases.

The additional cost, which is large when heparin is used, as well as the expense and inconvenience to the patient of daily determinations of coagulation or prothrombin time, does not seem justified.

We are indebted to Dr. Eugene Hildebrand for his assistance in evaluating the gross and microscopic lesions.

30 North Michigan Avenue

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tion, however, the outlet closes as the bronchus constricts, and air trapping distal to the foreign body develops. This is emphysema. When the foreign body has been in place long enough to block the bronchus completely, the emphysematous air distal to the foreign body is slowly absorbed, and collapse of that segment of the lung occurs. Expiration and inspiration films are a substitute for fluoroscopy. Fluoroscopic examination of a patient suspected of a foreign body in the bronchus is always indicated, because it is often difficult for the x-ray technician to obtain full expiration and inspiration films. On expiration, air leaves the one but not the other lung, which remains full and demonstrates air trapping in the main bronchus. Such expiration and inspiration films are diagnostic of a nonradiopaque foreign body in the main bronchus. Without bronchial obstruction a foreign body can be in place for a long time without infection. A pin, for example, may remain for years in the lung without causing trouble unless it perforates a vessel or creates granulations that block a

bronchus. It is bronchial obstruction that causes harm and permits infection to become rampant.

* * *

The diagnosis of a foreign body in the respiratory tract is easy when one remembers to think of the possibility. The story of the patient or that of the patient's family should be believed until proved wrong. X-ray examination should include the entire respiratory and digestive tracts. Fluoroscopy of the chest is indicated when a nonradiopaque foreign body is suspected. Unless a foreign body can be completely visualized, it is dangerous to attempt its extraction. The safe removal of a foreign body is aided by the possession of a duplicate, as well as x-ray study, so that its exact position and location are understood. Only then can removal be accomplished without the possibility of doing more harm than good through unwise manipulation. Extractions of foreign bodies are best done where there is an adequate armamentarium to deal with any complication that may arise.

BOSTON MEDICAL LIBRARY

Report of the President*

THIS annual meeting marks the end of my five-year tenure of the office of president, the first two having comprised the unexpired term of my predecessor and the last three the regular term prescribed by the by-laws. Since I could not accept renomination if it were offered, it is appropriate that I should render a brief account of my stewardship, with special reference to the state of the Library and to plans that are under consideration for its future.

First, I ask you to pay silent tribute to the following eight fellows who died during the year: Hugh Cabot, Charles H. Lawrence, Jr., Charles T. Porter, Abraham Rudy, Philemon E. Truesdale, Hugh Williams, Robert S. Hurlbut and Robert Sanderson. Worthy of note as examples of long-continued, loyal support are the forty-seven-year and forty-two-year memberships, respectively, of Dr. Cabot and of Dr. Truesdale. In this connection I am reminded of a physician who would not wish his identity to be known who, at the age of eighty-three and a fellow for many years and long retired from practice, submitted his resignation, on learning of our financial needs, however, he withdrew the resignation and doubled the amount of his annual dues.

Secondly, I have the privilege of making grateful acknowledgment, personally and on behalf of the Library, to the trustees and executive officers who have served with me, to the resident staff and to individuals and organizations who have continued

their loyal support. The Trustees, although they are busy with public and personal obligations, have served on committees and pooled their wisdom for our benefit, our secretary, our treasurer and above all our librarian have discharged their duties with no compensation except that of an approving conscience, and our resident staff, depleted in numbers, overworked and perhaps underpaid, under the directorship of Mr. James F. Ballard (now in the fifty-fourth year of his service) have serviced our collections and, so far as humanly possible, adequately met the needs of readers, students and researchers. The Massachusetts Medical Society, whose organ, the *New England Journal of Medicine*, is edited on our premises, and whose executive officers and committees share our building, brings us prestige and support in return for our services and help, likewise the *Journal of Bone and Joint Surgery* and many special societies make use of our facilities to our mutual advantage.

The last five years comprise the entire period of the participation of our country in World War II, together with the months of disruption of normal peaceful activities immediately preceding and succeeding it. Perhaps a total world war is sufficient excuse for any enterprise such as ours not only to fail to advance but also to develop structural and functional weaknesses. Friends of the Library who have read the reports of the president and of the librarian for the last four years are familiar with the matters that have preoccupied us, among which are the conversion of our heating system from oil

*Presented in part at the annual meeting of the Boston Medical Library March 5, 1946.

heaved that there was a wheel from a plastic toy lodged in the hypopharynx and therefore suggested sending the child to the hospital for removal. The mother demurred and called a second physician, who said that with a tongue depressor he could see a disklike object in the hypopharynx that could be grasped with the fingers but could not be dislodged. After unsuccessful efforts for an hour with a can of ether, a flashlight, a tongue depressor and the fingers, the child was taken to the Massachusetts Eye and Ear Infirmary, where a laryngoscope and forceps were requested, to remove the disk, which had some sort of protrusion on its inferior surface. X-ray films were taken in spite of the fact that the physician considered them unnecessary. The films demonstrated the eye of a toy bear imbedded, with the large end in the hypopharynx and the pointed portion, used to hold the eye in the bear, penetrating the pharyngeal wall and extending down into the soft tissues of the neck. In the pharynx above the eye, a laceration about 2.5 cm long and 0.6 cm wide was observed. Manipulation had resulted in a tremendous amount of air emphysema in the soft tissues of the neck, this extended into the mediastinum around the heart and up to the base of the skull. After extraction of the foreign body and the administration of penicillin and sulfadiazine the patient made an uneventful recovery. This case emphasizes the value of x-ray examination and the fact that extreme caution must be observed in manipulating a foreign body.

A foreign body in the larynx is rare. If a foreign body of any appreciable size lodges in the larynx, the airway is obstructed and the patient dies promptly, before help can be given. The object, however, may be small enough so that the patient can breathe around it, but whenever a foreign body prevents the vocal cords from approximating normally, hoarseness results. It is too often forgotten that hoarseness means trouble with the organ of speech, the larynx. A case in point is that of a twelve-month-old child with a history of increasing cough and hoarseness of four weeks' duration in which x-ray examination demonstrated a safety pin between the vocal cords. It was apparent from these films that the pin was pointed up and that the point was imbedded anteriorly in the base of the epiglottis. When I saw this x-ray film, I doubted the mother's statement of four weeks of hoarseness. The larynx was exposed without anesthesia, and it was seen that the blackened, corroded head of a safety pin in the posterior portion of the glottis was almost completely surrounded by red granulation tissue. I attempted to remove this pin by grasping the head and holding the point with the tip of the laryngoscope. After carrying out this procedure, I discovered that I had the head and the back of the safety pin, but that the spring and the pointed end were missing. Inspection of the larynx did not reveal the remainder of the pin. The child was taken

to the x-ray room, where films demonstrated the remainder of the pin in the right main bronchus. A bronchoscope was inserted, and the portion readily removed. The corrosion and brittleness of the pin offered sufficient proof that the mother's statement regarding the four weeks' duration was reliable. Without the x-ray examination and many pieces of equipment, this case might have been difficult. Thus, it is essential that the removal of any foreign body from the larynx or below be done in a hospital equipped to deal not only with the particular situation but also with all possible complications.

Foreign bodies in the trachea challenge diagnostic ability, unless they are radiopaque, when they are easily diagnosed by x-ray examination. But the diagnosis of a nonradiopaque foreign body in the trachea is made by the history and physical signs. Even in the youngest children, the pathognomonic signs are a sudden stopping of the expiratory air blast, with cessation of phonation and paroxysmal cough, followed by relief with a good airway and good phonation. Large seeds or shells of nuts produce these signs. Recently, a three-year-old child coughed and choked when he fell while eating. He was taken to another hospital, where a variety of studies, including x-ray films, were carried out. He was discharged and then returned to the hospital for a stay of another week. Periodically he had attacks of cyanosis associated with coughing and wheezing, and because of one of these he was rushed to the Massachusetts Eye and Ear Infirmary for an emergency tracheotomy. On arrival, the signs had subsided. Shortly after admission, they recurred and then disappeared. A large piece of pistachio-nut shell was removed from the trachea through a 5-mm bronchoscope, and the child was subsequently symptom free.

Foreign bodies that are aspirated usually do not move up and down in the trachea but become lodged in one of the main bronchi or, if small, go farther into one of the smaller bronchi. It is not so much the actual diagnosis of foreign body in the bronchus that is difficult as it is the consideration of the possibility. The physician not only forgets to ask about the possibility of a foreign body but also, too often, fails to believe the patient's own story. An x-ray film, which is easy to take and inexpensive, often explains an atypical case of pulmonary disease. The physical signs of bronchial obstruction are well known. In time, bronchial obstruction leads to suppuration, with fever, chills, cough and sputum. Although an x-ray film of the chest leaves no doubt that a radiopaque foreign body is present, it is equally effective in revealing nonradiopaque objects that have been in place for a long time. If a foreign body causes only narrowing of the bronchial lumen, a wheeze is the cardinal sign. Irritation of the bronchial tissues by a foreign body results in swelling and a further narrowing of the lumen so that air passes the foreign body on inspiration, with dilation of the bronchus, on expira-

Society and by various committees and other groups. At present the Society's executive offices and the editorial rooms of the *New England Journal of Medicine* are in our building, an arrangement that contributes much to the efficiency and prestige of both.

The exact nature of the proposed alliance will require careful study. Many of the older fellows would be sorry if the Library lost anything of its distinguished identity, a misfortune that could not occur to the Society. The Library has assets valued at between one and two million dollars, depending on the appraisal of irreplaceable files and memorabilia. It is a corporation, and the title of its property is vested in the fellows, who constitute the corporation and whose dues are an important source of income. Nearly all the fellows of the Library are members of the Society but about four fifths of the latter are not fellows of the Library, although they would be perfectly eligible if they so desired after the formality of proposal for membership and action by the Committee on Elections had been complied with. If the Society wished to make a substantial annual contribution to the support of the Library, the comparative status of members of one and fellows of the other would require definition and adjustment. As a matter of fact, the Library has always extended a warm welcome to all reputable

physicians — indeed to all citizens — to use freely its facilities and enjoy its privileges, except only those necessarily pertaining to actual ownership or to its status as trustee under wills and bequests.

This is not the place to elaborate on the legal and practical problems raised by this plan. If its realization seems wise, these problems can be solved by men of good will. The broad and liberal view seems to be that we have two organizations whose purposes are essentially identical in striving to promote the public health, each with an enviable record of unselfish service over many years. One has a plant and collections of stored medical knowledge second to but few in this country but lacks endowment and other income adequate for its support, the other, through its numerical strength and wide influence, is able to contribute that support. As one who for nearly forty-five years has been active in the affairs of both these organizations and who has the deep conviction that the prestige and strength of each would be promoted by a close alliance, I have no hesitation in urging that its feasibility be explored to the end that its consummation be accomplished at the earliest possible moment, for time is of the essence now that, after the disruption of War, the institutes of peace are to be restored.

DAVID CHEEVER

Report of the Librarian*

WITH the end of the war and the return of men from the services, the Boston Medical Library is slowly regaining the position it held five years ago. By the beginning of 1946 the membership had already increased and had reached a total higher than that at any time in the history of the Library. During the year, the staff remained unchanged and the Library continued to function at a decreased pace but serving its clientele in what appears to have been a reasonably satisfactory manner. At least no major complaints were heard by the librarian and although many of our services were, of necessity, restricted and we were cut off almost entirely from foreign medical literature, books as well as periodicals, we extended our holdings in English-language periodicals and made an attempt to keep abreast of the times. Much of our foreign-language material, which is being stored abroad, will presumably be made available to our readers in 1946. The German material is entirely lost, but it is quite possible that the paper on which it was printed was so inferior that binding would not have been advisable, these missing periodicals may now be reprinted or duplicated in some form on better paper so that they will have a chance of survival.

The librarian thought the time fitting to give a brief review of the various departments of the Library, covering a period of ten or more years. A discussion and tables on periodicals, binding, membership, use of the Library and size of the Library are therefore included in this report, in addition to the usual departments of book reviews, publications and a statistical evaluation of the contents of the Library as of December 31, 1945.

THE LIBRARY FROM 1936 TO 1945

Periodicals

The current medical literature is largely in periodical form, and the greatest use of a library such as ours is found in this department. The total number of periodicals received in 1945 was 578, only 44 being in languages other than English. Our average from 1930 to 1940, before the war, was about 800 to 900, in 1930, for example, we received 870, and 410 (nearly 50 per cent) were in foreign languages. Since about 1937, by arrangement with the Harvard Medical School Library, we have specialized in clinical journals. It, in turn, has expanded into the fields of public health, dentistry, biology, basic sciences and ophthalmology (Howe Library). This collaborative effort reduced our total number of

*Presented in part at the annual meeting of the Boston Medical Library March 5 1946.

to steam, structural alterations to meet the needs of the Massachusetts Medical Society and the *Journal of Bone and Joint Surgery*, the establishment of the James F. Ballard Publication Fund, the issue of a catalogue of our incunabula and manuscripts and the promotion of an elaborate survey of the various medical libraries in Boston. But also since the beginning of the administration of my predecessor, or for at least twelve years, your officers have been anxiously occupied with the problem of conducting a dynamic and expanding enterprise under the handicap of originally inadequate and steadily diminishing financial resources. The Library, ranking second or third in the United States in the value of its collections and the potential importance of its services, is conducted with heart-breaking economy on a yearly income of about \$30,000. It should have resources of at least double that amount, together with a corresponding capital sum for completing and improving our still unfinished house. We are seriously in arrears in the purchase of current texts, in subscriptions to periodicals, in binding and rebinding and in cataloguing, and there is literally no room for accessions except temporary installations in the basement and corridors. Only the invincible optimism of our librarian, Dr. Viets, and the efficient industry of Mr. Ballard and his staff have kept up our courage and maintained the library service so well that there have been scarcely any complaints. The details of our physical condition have been so well presented in previous reports that they may be omitted here.

It is the almost unanimous opinion of your officers and their advisers that the provision of facilities for the collection, housing, circulation and preservation of the literature of the medical and allied sciences in any geographic area should be conceived on broad principles of co-operation and mutual assistance among the various interests involved, instead of the individualistic development of a number of essentially similar units all situated within a mile or two of each other. At the turn of the century, when ours was the only considerable collection in this vicinity, it seemed reasonable that the library should continue its independent career, supported by bequests and gifts and by its fellows and members. Later, a plan to build about it as a nucleus an elaborate academy of medicine, enthusiastically advocated by a group who went so far as to secure an option on land and to obtain an architect's services, was reluctantly given up because of the expense involved, which ran into millions of dollars. During this time there came into being the working libraries of Boston University, Harvard and Tufts College medical schools, as well as the libraries of several major hospitals and numberless small collections of individual investigators and teachers, one of these is well known actually to rival our library in size and usefulness. The survey and resulting plan, designated by us as the "Fleming-Metcalf Plan," which

aimed to integrate and develop these elements into a co-operative and mutually beneficial system, has been approved by the authorities of the three medical schools and its consummation actively pressed by your officers. Briefly, the plan envisaged the gift of a large sum by a charitable foundation for capital expenditure, the raising by the Library of a similar sum by subscription among the medical profession and other friends for endowment and the contribution annually of substantial contributions by the working libraries of medical schools and hospitals in return for our service as a central reference and research library ready to supply the needs of the smaller units beyond those of the everyday requirements of faculty, students and staff, and to make unnecessary the expensive enlargement of their physical plants. This plan had the invaluable support of Mr. Metcalf, Director of Libraries of Harvard University, and the tentative approval of the administrators of the three medical schools. Unfortunately, the members of the foundation, although approached by one who had their ear, found themselves unable to embrace the opportunity. Several other sources were unresponsive. Your officers and committees reluctantly concluded that without this aid the project as planned could not be realized.

Another plan is now under consideration—one that for some years has been tentatively suggested and as often put aside as possibly presenting peculiar difficulties. It is nothing less than a proposal of honorable marriage to a contemporary of the Library, quite similar in age, outlook and ambition for future accomplishment. Perhaps, since the prosecution of this suit must rest in the capable hands of my successor, I should not mention it, but after all I have sat in at preliminary talks among the old folks and it is well that the community should get used to the idea.

The Boston Medical Library and the Massachusetts Medical Society have much in common. Perennially young though they may be in spirit, they are perhaps the oldest of their kind in the country, if we date the former from the Second Social or Boston Medical Library, organized in 1803 by the Medical Improvement Society, under a statute of 1798. The statements of their aims as inscribed on their charters are practically identical. The fellows of the Library are almost without exception members of the Society. In 1876, when the Library moved from its two rooms in a basement in Hamilton Place, furnished with two tables, thirteen chairs and some bookshelves, to a little remodeled house at 19 Boylston Place, among the distinguished speakers at the dedication ceremonies was Dr. George H. Lyman, president of the Society. Soon the books accumulated by the Society—1500 in number—were turned over to the Library. Almost from the first the Council of the Society met in the meeting hall, followed by the Suffolk District Medical

from 17 in 1944 to 31 in 1945, is directly attributable to the energetic work of the Membership Committee.

SPECIAL ACCESSIONS

As usual our restricted funds for special types of books were expended for the purposes designated

to be diverted into channels other than the more frequent one of acquiring the latest texts and monographs. This we also do, so far as our income permits. More funds are urgently needed for current literature, and until we have them some fields of medical advance will not be fully covered by our accessions. We are relatively strong in our chosen

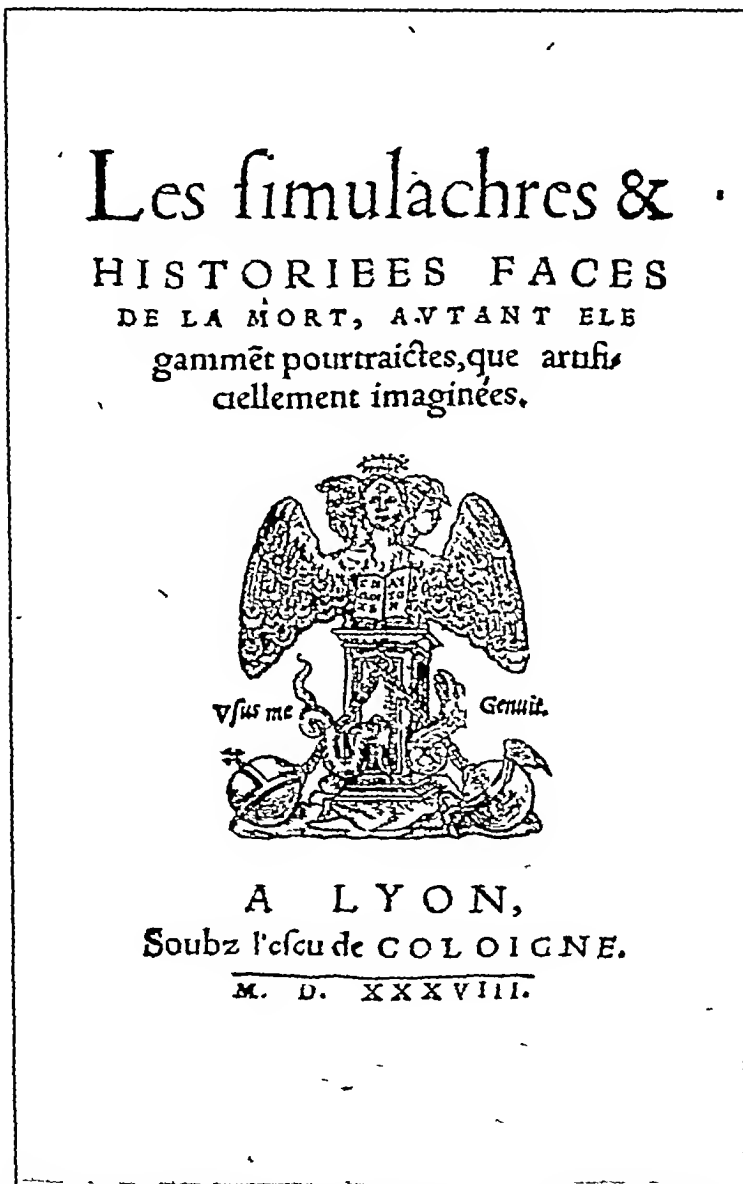


FIGURE 1 Title Page of *Les simulachres & histories faces de la mort*, by Hans Holbein (Lyon, 1538)

by the various donors. That a considerable portion of our book funds are so entailed leads to a belief that the Library is primarily an antiquarian institution, with little interest in current medical literature. This is not the case, although we are particularly fortunate in having more funds than most libraries

field, clinical medicine, and by co-operation with other libraries all fields are fairly well covered in the Boston area. In the special groups, however, we have continued to buy a considerable number of important books, and in some cases to catalogue previous purchases.

periodicals by about 100. During the war, with most of the foreign journals omitted, the number fell as low as 466 in 1944. In 1945 the number of periodicals increased to 578, without most of the more than 400 foreign journals previously received. We have some reason to suppose that our back files of foreign-language journals, except for the German periodicals, are intact in Europe and awaiting shipment to Boston. Our stock of German journals was probably lost by bombing. According to our latest information, the French, Italian, Dutch and Scandinavian periodicals are awaiting clearance and shipping space. Russian journals are now arriving in good number by way of exchange. When we know the cost of our foreign-language stock now abroad, we shall again ask aid from the special societies, which have made generous donations in the past for this purpose.

About 150 journals come to us each year from the *New England Journal of Medicine*, received by them in exchange. When the paper shortage is less and a greater number of issues of the *Journal* can be printed, this list may be expected to increase. The Library could use 50 or more subscriptions of the *Journal* to advantage, and the editor, as always, extends a generous hand in our direction.

Binding of Periodicals

Until about 1937 the Library bound nearly all the periodicals received each year—a total of approximately 900 volumes. Since that date we have had to curtail this activity for financial reasons and now only bind in permanent form 50 to 60 per cent, the others going into temporary binders. Thus, in 1945, only 360 of the 578 periodicals received could be bound. This is naturally disturbing to the librarian, and although it does not preclude the use of these journals, a backlog of journals requiring binding is being built up that we can hardly afford, if the Library is to remain in a workable condition. Since the periodical files are used more than any other division of the Library, permanent binding is almost essential.

Size of the Library

The number of books in the Library slowly approaches 200,000, a total of 199,135 being reached in 1945. The collection of pamphlets, numbering 135,195, grows only gradually, since reprints of papers occurring in the current literature are no longer catalogued. Nearly 3000 books, including 700 bound volumes of periodicals, and over 1000 pamphlets were added in 1945. To catalogue these items, more than 10,000 cards were used.

Plans must shortly be made to provide additional space for our growing collections. This could be done in a number of ways. We have room in our own building for seven more tiers of stacks, which should be built, if funds could be found, for this would be a natural way to house our collection. Secondly,

we might transfer the 10 to 20 per cent of our collection that is seldom used to the Harvard University Deposit Library. The cost of storage is relatively low, and items so stored can be removed for use in the Library in a few hours. Thirdly, if a new library is provided in the near future for the Army Medical Library in Washington and it is allowed to become a national medical library, with appropriate borrowing privileges extended to us, we might take from our shelves certain rarely used material, particularly in the nonclinical sections, and deposit it in Washington.

All these plans have good features, and some use of each is probably the best method of handling the problem. By 1950 the librarian hopes to see the stacks completed, some of our collection transferred to the Harvard University Deposit Library, our basement cleared of duplicates and our arrears dissolved. If someone will give us the tools, in the form of funds, the staff, augmented by new personnel, will do the job.

Use of the Library

Both the circulation—that is, the number of items taken from the shelves for use by readers—and the attendance increased in 1945 over 1944, the former from 29,949 to 31,298 and the latter from 7021 to 7100. The circulation in 1945 was approximately that of the average for the last ten years, but we have had during this period, for some reason not fully explainable, a wide swing from about 25,000 to 47,000. The attendance in 1945 was only about 70 per cent of its normal level of 10,000 a year, but it is expected that, with members rapidly being demobilized, the number will rapidly increase. If 10,000 readers use 35,000 items in a year, the Library, as now constituted, is giving a reasonable service. The space for reading in Holmes Hall and elsewhere is rarely used to its limit, since most members call for books and periodicals to use at home or in the office. About 7 out of 10 readers using Holmes Hall are nonmembers.

Membership

The total membership in the Library rose to a new height in 1945, the figure being 932. Fellows constitute about 70 per cent of this total. We have been slowly increasing our membership since 1930, particularly in the years since 1937. There is nothing artificial about our growth, and the increase in numbers indicates a healthy condition, in spite of our numerous and indeed obvious weaknesses. It is hardly a sign of decadence when an increasing number of doctors find it profitable to use the Library and to pay for doing so. The growth speaks well, moreover, for the continued success of the active Membership Committee, but I doubt if even they could hold the membership to its present level if the Library did not offer a reasonably good service. The large increase in the professional members,

in 1507, and a third, in 1517, was particularly grave in Oxford and Cambridge. In 1528 another epidemic occurred in London, driving the court of Henry VIII from his residence. From England it spread to Europe, first to Hamburg and then into France and Italy. The so-called "English sweat" never appeared in Europe thereafter, but an epidemic in England, in 1551, was described by John Canus in his famous book published in 1552.

The Library added an account of this disease published within two years of the Hamburg outbreak, which began on July 25, 1529. Joachim Schiller, born at Herdern, near Freiburg, was in practice when he published, in 1531, *De Peste Britannica* (Fig. 3). The European epidemic ended in Novem-

ber, 1501, a treatise on syphilis entitled *Malum Francie*, which has been acquired by the Library. He was, of course, writing from Ulm, in Germany, and used the common appellation of the time. His book, published in Hagenau, appears to be rare, since only one other copy is recorded, in the library at Zwickau (at least it was so noted before World War II). It is interesting that the manuscript from the Ulm physician crossed the Rhine to be printed in Hagenau by Heinrich Gran, a well known printer of fifteen-century medical books. The syphilis tract is a brief account of five pages.

Hugo Senensis (Ugo da Siena) was one of the most prolific of the medical writers of Italy. He taught at Siena, Bologna, Parma and Pavia and gave lectures at the Sorbonne. One of the earliest physicians to write in the common tongue, his *Trattato* is a justly celebrated incunabula, first printed at Milan in 1481. The original edition is in the Library (No. 383 in the Ballard catalogue³). A later printing (Milan, 1508) in Latin was added to the Library in 1945, with an interesting woodcut on the title-page depicting doctors and astrologers in consultation (Fig. 4).

English Imprints

Seven books, printed in London before 1640, were added. One was a partially recorded early printing, probably the first edition, of a work by J. Fletcher entitled *The Differences, Causes, and Judgments of Urine* (Cambridge, 1598). There is an imperfect copy in the library at Cambridge, England.

Spanish Imprints

Nine books were added to this class, including a treatise on physiology written by the Mexican, M. J. Salgado, in 1727.

Americana

Of particular interest are the *Armory Square Hospital Gazette*, published by a Washington hospital in 1864-1865, the *Medical Inquirer*, a botanic journal issued in Fall River and Middleboro in 1846-1847, Joseph Warren's 1772 and 1775 "Oration" and an engraved card, "Entitles to Kine Pock Inoculation," signed by Benjamin Waterhouse.

Modern Manuscripts

The *Letter Books* of Julius Griffiths, in four volumes (1810-1829), and the *Records of the Rutland County Medical Society*, 1816-1829 (Rutland, Vermont) were added.

Incunabula

Three incunabula were added, two of which are not recorded in the Stillwell *Second Census*: the *Commentaria in Platonem*, by Marsilius Ficinus (Florence, 1496), and the *Quaestiones Naturales* (Cologne, circa 1500).

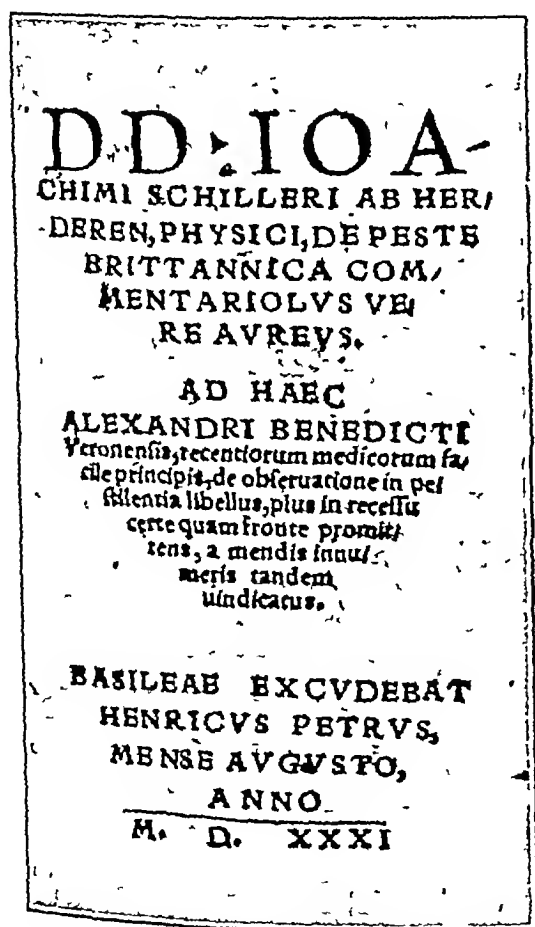


FIGURE 3 Title Page of *De Peste Britannica*, by Joachim Schiller (Basle, 1531)

ber, 1529, apparently as rapidly as it had begun. Schiller's work, a pamphlet of twenty-five leaves, is a scholarly discussion of the disease, without much historical importance. He gives no real description of the epidemic of 1529.

Otto Raut, an astrologer, who issued a prognostication for the years 1502 and 1503, also wrote,

Sixteenth-Century Imprints

Among the foreign imprints of the sixteenth century, we have acquired *Les simulachres & historiees faces de la mort* by Hans Holbein (Fig 1). This book, the first edition of Holbein's *Dance of Death*, was published in Lyons in 1538. It is illustrated with forty-one small woodcuts, as fine as copper plates, probably made from Holbein's drawings by Hans

Often reproduced in medical literature is the drawing of the skeleton, Death, calling on the physician in his study (Fig 2). Beside the doctor lies his dog. Death leads in an elderly, sick man for consultation with the physician, bringing the urine bottle for casting. The sharp-nosed doctor is not perhaps our ideal physician, but he is obviously a student and the old man, the patient, is a figure

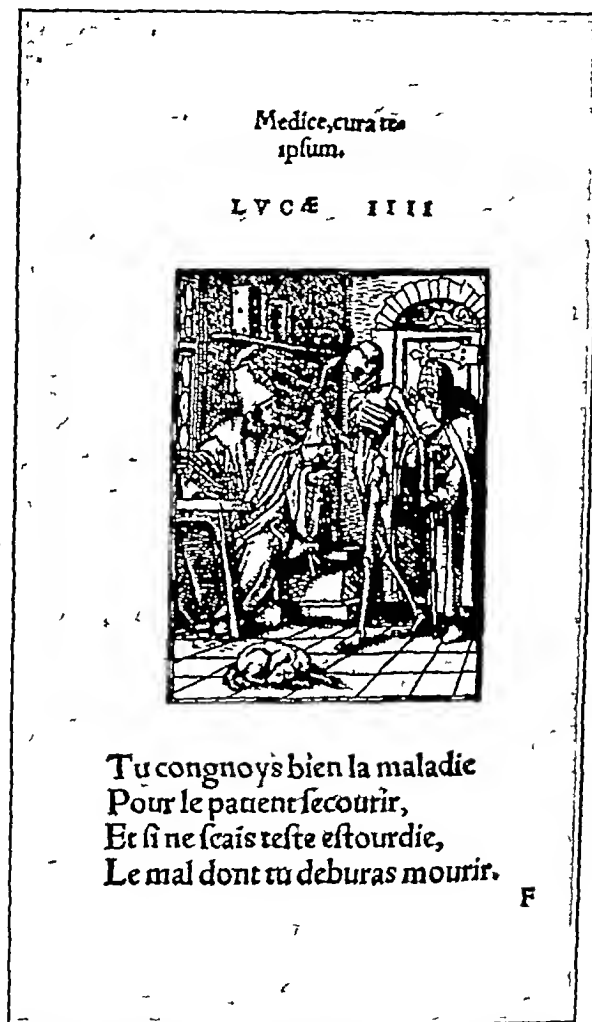


FIGURE 2 Holbein's Drawing of the Physician, Death and an Elderly Patient in the First Edition of *Les simulachres & historiees faces de la mort* (Lyons, 1538)

Lützelburger Warthin,¹ who describes the book in detail, although with a number of errors, states that more than a hundred editions, as well as copies and imitations, are known, following this first printing in book form in 1538. The *Totentanz* or *dance macabre* was a favorite subject for the Renaissance illustrators, and Holbein's figures, or imitations of them, occur frequently as initial letters in books of the sixteenth century

of great charm. Warthin describes Holbein's technique as follows:

In the Holbein cycle the art of the *Totentanz* motive reached the highest point of its development. Nothing has since approached it, either in inspirational value, human interest, or in skill of technique.

The sweating sickness, a fatal epidemic disease running a rapid course, first appeared in England in 1485.² A second, less severe epidemic was noted

Editorial Medical classification scheme of Boston Medical Library *New Eng J Med* 232 532, 1945

Editorial Doctor illustrates his travel notes *New Eng J Med* 232 437, 1945

Editorial Medical bibliography *New Eng J Med* 232 686, 1945

Sixty-ninth Annual Report of the Boston Medical Library for the Year 1944 36 pp Boston privately printed, 1945

Editorial Boston Medical Library *New Eng J Med* 233-542, 1945

Cheever, D Report of the president, Boston Medical Library *New Eng J Med* 233 520, 1945

Viets, H R Report of the librarian, Boston Medical Library *New Eng J Med* 233 521-527, 1945

Editorial Albrecht Dürer and anatomy *New Eng J Med* 233 605, 1945

Editorial Marion Sims and his silver sutures *New Eng J Med* 233 631-633, 1945

Viets, H R *A Museum in a Medical Library* 7 pp Boston privately printed, 1945

Miscellaneous

There were no staff changes in 1945, our six regular employees continuing to give the best service possible under restricted conditions. Ten, or possibly twelve, people are needed to run the Library in a satisfactory manner.

The Massachusetts Medical Society, the Boston Society of Psychiatry and Neurology, the Suffolk District Medical Society, the New England Heart Association, the Boston Surgical Society and the Boston Medical History Club met, as usual, in the Library.

Our cordial relations with our close associates in the building, the Massachusetts Medical Society, the *New England Journal of Medicine* and the *Journal of Bone and Joint Surgery*, were maintained.

The director and the librarian attended meetings of the honorary consultants of the Army Medical Library, Washington, D C, and the librarian delivered an address at the dedication of the Ditttrick Museum in the Cleveland Medical Library on October 6, 1945.

HENRY R VIETS

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- 2 Hecker J F C *The Epidemics of the Middle Ages* 380 pp London Sydenham Society 1846
- 3 Ballard J F *A Catalogue of the Medical and Renaissance Manuscripts and Incunabula in the Boston Medical Library* 246 pp Boston privately printed 1944

MEDICAL PROGRESS

DISEASES OF THE THYROID GLAND*

SAMUEL L GARGILL, M D,† AND MARK FALCON LESSES, M D‡

BOSTON

SINCE 1942, when the last review of this subject appeared in the *Journal*,¹ there have been many important advances in the understanding of the biochemistry and physiology of the thyroid gland. In addition, a new group of substances that are goitrogenic and at the same time markedly depress thyroid function have been extensively investigated. Radio-iodine, which has been widely used in the investigation of thyroid physiology and iodine metabolism, has reached the stage of clinical usefulness in the treatment of toxic goiter. The value of blood iodine studies continues to be demonstrated, with chief emphasis on the protein-bound iodine of the serum. Finally, there has been further study of the cause of exophthalmos in animals, as well as some clarification of the clinical problem involved.

THE THYROID HORMONE

The diverse actions of the thyroid hormone on bodily functions are fairly well known, but the

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exact chemical nature of the hormone and the mechanism of its biosynthesis have not been completely elucidated. It has been established that the hormone itself lies somewhere between the large molecule protein, thyroglobulin, and the relatively simple, iodine-containing amino acid, thyroxine, if in fact it is not either. Harington² has contributed new evidence that favors the view that the circulating or effective form of the hormone is thyroxine. It has long been accepted that thyroxine produces every symptom of clinical hyperthyroidism except exophthalmos and conversely is capable of relieving every symptom of myxedema, whether clinical or experimental. It has not been possible, however, to demonstrate a direct effect of thyroxine on normal surviving tissues in acute experiments of several hours' duration. Craig and Salter³ believe that the thyroid hormone is not thyroxine because of the failure of thyroxine, when added to normal blood, to induce the calorigenic action in excised surviving tissues that was readily produced by the blood of thyroxinized animal. The authors themselves remark on the high degree of variability in their data but consider their conclusions statistically valid. In addition, the physiologic activity of the thyroid

LIBRARY ACTIVITIES

Book Reviews

Owing in part to the fact that many of our regular reviewers were still in the service, only forty of the

Exhibits

During 1946, the following exhibits were set up in the entrance lobby of the Library

Röntgen, Konrad In commemoration of the fiftieth anniversary of the discourse of the x-ray (November 8, 1895)

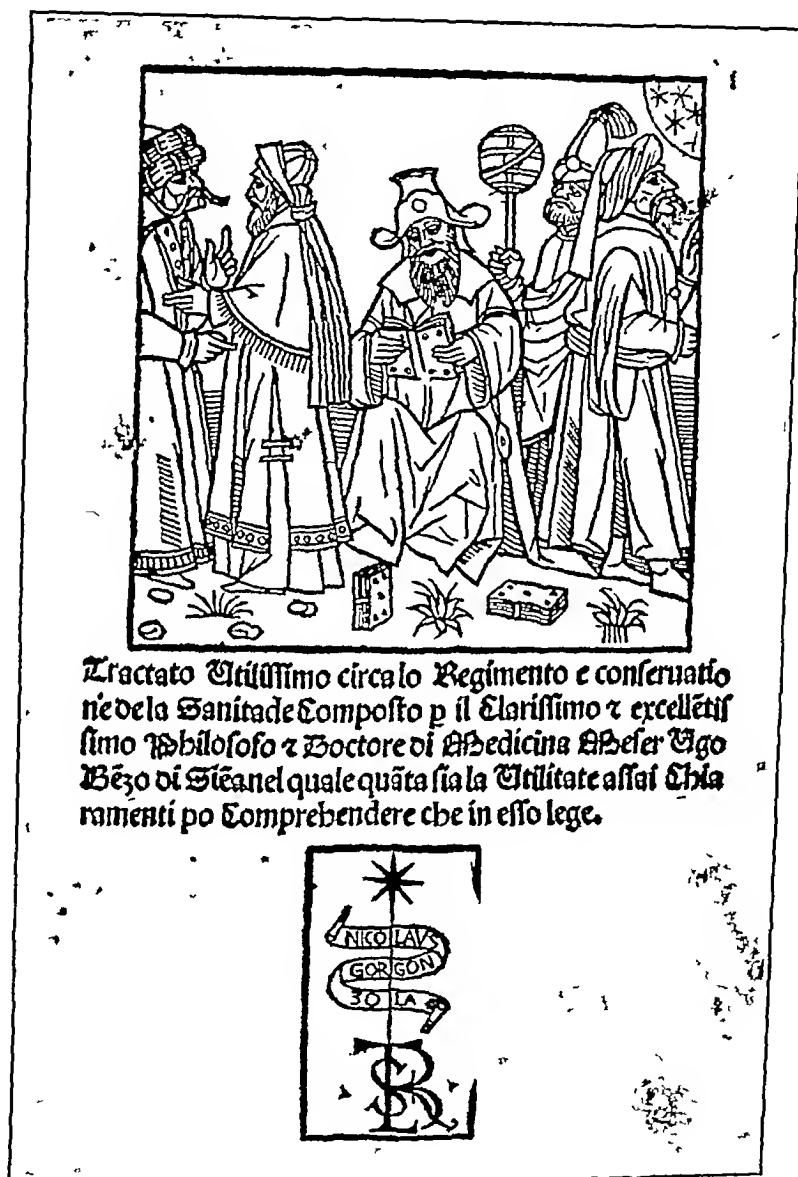


FIGURE 4 Title Page of *Tractato Utilissimo circolo Regimento e conservatio de la Sanitade*, by Hugo Senensis (Milan, 1508)

two hundred and twenty-six books received from the *Journal* in 1945 were given extended review notices. The other hundred and eighty-six were allotted short reviews or summaries. Eighty-three reviewers, whose names are listed in the two annual index numbers of the *Journal*, gave a valuable service to the Library. Mr. Ballard, as in the past, carried the brunt of the work on the short notices.

Dürer, Albrecht An exhibition of five editions of his book *Human Proportion*, including the first edition (Nuremberg, 1528).
Cornwall, Dean Series of paintings of outstanding American medical events.

Publications

Recent articles emanating from the Library are as follows

workers¹⁹ have repeatedly shown that with tracer doses almost all the radio-iodine deposited in the thyroid gland is organically bound within an hour.

When large amounts of radioactive iodine are added to the medium in which surviving thyroid tissue slices are respiring, there is rapid incorporation of the radio-iodine in the tissue. As in the experiments *in vivo*, the radioactivity is first associated with di-iodotyrosine and later appears with thyroxine, indicating the same process of conversion as in the intact animal.^{21, 22} It is of interest, however, that Schachner, Franklin and Chaikoff²³ demonstrated that surviving thyroid slices were able to concentrate up to 60 per cent of added radio-iodine even after the inhibition of thyroxine and di-iodotyrosine formation by azide or sulfanilamide. Cyanide and sulfide, in addition to inhibiting thyroxine and di-iodotyrosine formation, blocked the accumulation of radio-iodine by thyroid slices. From this selective blocking of iodine concentration and thyroxine formation, the authors concluded that thyroid tissue possesses a mechanism for concentrating iodine that does not depend on conversion of inorganic iodide to thyroxine and di-iodotyrosine.

This group of investigators²⁴ has directed attention to the importance of an enzyme system in the biosynthesis of thyroxine, first by demonstrating that homogenized thyroid tissue has lost its capacity to incorporate radioiodine, thus proving the need for cellular organization, secondly, by showing that the incorporation does not occur with complete anaerobiosis, and thirdly by blocking di-iodotyrosine and thyroxine formation from inorganic iodide in thyroid slices by typical inhibitors of cytochrome oxidase, such as cyanide, azide, sulfide and carbon monoxide. Dempsey²⁵ has demonstrated the presence of cytochrome oxidase in the cells of the thyroid follicle and has also presented evidence for the presence of peroxidase in the thyroid cells. He found that the peroxidase reaction was easily inhibited by thiouracil, whereas the cytochrome oxidase reaction was unaffected. This has been confirmed by DeRobertis and Grasso²⁶ regarding peroxidase activity and the inhibitory effect of thiourea.

Harrington and Pitt Rivers¹⁵ postulate that the enzymic oxidizing system liberates iodine from iodides and this free iodine is the effective oxidizing agent that both converts tyrosine to di-iodotyrosine and vice versa. Keston²⁷ lends support to this view by the demonstration that iodine and oxidases participate in the reaction that organically binds iodine. Recently, Remeke and Turner²⁸ after a study of the factors influencing the iodination of casein, concluded that manganese is probably also an important catalyst that acts in promoting thyroxine formation *in vivo*. Ray and Deysach²⁹ had earlier shown the particular ability of the thyroid to store manganese. The biosynthesis of thyroxine

is thus seen to be intracellular, aerobic and enzymatic.

The effect of hypophysectomy on thyroxine synthesis in the organism has also been studied with the use of tracer doses of radio-iodine.²⁰ The incorporation of iodine into the thyroid gland was much slower and in lesser amounts in hypophysectomized animals. The conversion of iodide to di-iodotyrosine was unimpaired, but the formation of thyroxine was greatly diminished or almost inhibited.

The extrathyroidal production of thyroxine or thyroxinelike substances by iodination of proteins in the test tube has directed attention to the possibility of a similar synthesis in the thyroidless organism. Chapman³⁰ found that the level of iodine intake had a significant effect on the weight, surface area, metabolic rate and food utilization of thyroidectomized animals, those with higher iodine ingestion showing an effect that suggested to the author that iodine might play a role in the production of a thyroxinelike substance in the tissues. This aspect of extrathyroidal hormone production was firmly established by Chaikoff and his collaborators³¹ through the use of radio-iodine as an indicator. From two to eight months following thyroidectomy, radio-iodine was injected into young rats, which were then killed at intervals of two to ninety-six hours after the injection. The liver, muscles and small intestines showed measurable quantities of labeled thyroxine and di-iodotyrosine. The completeness of the thyroidectomy was checked both by serial section and by the radio-autographic technic. These experiments indicate that tissues other than the thyroid maintain a primitive ability to elaborate a thyroidlike substance. This is confirmation of the concept of Means³² regarding the priority of the hormone over the gland in the evolutionary scale, the evolution of the gland representing a more efficient method of hormone production.

THE ANTITHYROID GOITROGENS

Compounds that possess antithyroid properties fall into two general categories: those that act without producing goiter, of which iodine and radioactive iodine are examples, and those that cause marked hyperplasia and at the same time depress thyroid function. The latter embrace the cyanides, thiocyanates, sulfonamides and thiourea, with its derivatives. This subject has been extensively reviewed by Williams³³ and by Riker and Wescoe.³⁴

The goitrogenic action of cabbage, demonstrated in 1929 by Chesney, Clawson and Webster,³⁵ was shown by Marne et al.^{36, 37} to be common to the entire genus of Brassica and to be due to contained cyanides. The condition produced was in essence an iodine-deficiency goiter, since it could be prevented by administered iodine and was due to

gland has been claimed to parallel its total iodine rather than its thyroxine iodine content.⁴ Although Harington dismisses the evidence as scanty, if true, it invalidates the hypothesis that thyroxine is in fact the circulating hormone and has directed attention to the parent protein, thyroglobulin, or a peptide derived therefrom.

Sensitive immunologic precipitin tests,⁵ however, have failed to reveal circulating thyroglobulin, which is active orally in the thyroidless animal. If it were the true hormone one would therefore have to assume that after its degradation for absorption by the intestinal tract it was resynthesized in the absence of the thyroid gland. More direct evidence excluding thyroglobulin itself as the circulating hormone has been offered by Bassett, Coons and Salter,⁶ who found the major part of the circulating iodine in the albumin fraction, although the highest concentration of iodine was in the alpha and beta globulins.

Harington² presents immunologic experiments that strongly support his view that thyroxine is the thyroid hormone. He immunized animals with thyroxine-protein complexes, whose antigenic specificity was determined by thyroxine and di-iodotyrosine groups, to produce an antiserum whose antibodies were specifically adapted to combine with the molecule of the physiologically active substance and consequently to interfere with the action of this substance in another animal by a process analogous with passive immunization. The antisera thus developed against the artificial thyroxine proteins did not lower the metabolic rate of normal animals, but they did prevent, almost completely, the characteristic rise in metabolic rate caused by the administration of either thyroglobulin or thyroxine. This neutralization of the effect of thyroxine by the antisera showed that the circulating antibodies, which contained combining sites adapted to thyroxine, interfered with the access of the latter to its normal sites of action in the tissues. This conclusion is supported by earlier work of McClendon and his associates,⁷ who found that the calorogenic action of thyroglobulins from goiters of all types depended on their thyroxine content only and concluded that this content rather than total iodine determined calorogenic effect.

If the circulating hormone is thyroxine or some other hydrolytic product of thyroglobulin, the gland itself should contain an enzyme system capable of breaking down thyroglobulin by proteolysis into smaller components that can pass across cell membranes. The existence of such an enzyme system has been demonstrated and its activities quantitated by DeRobertis and Nowinski,⁸ who found a 100 per cent increase in proteolytic activity in the thyrotoxic gland as compared to the normal, and a 25 per cent decrease in iodized thyrotoxic glands and in nontoxic diffuse goiters.

Meyer and his co-workers,⁹ by injecting thyroglobulin, produced an immune serum that was effective in producing passive immunization against thyroglobulin in normal rabbits as determined by a reduction in the metabolic rate and the prevention of an increase in metabolic rate from injections of the same thyroglobulin used as an antigen.

Thyroxine synthesis had been accomplished in the laboratory by Harington and Barger¹⁰ in 1927. Proof of the steps in the biosynthesis of thyroxine has been furnished by radio-iodine studies. The progression from the iodine-free amino acid tyrosine to the physiologically active tetra-iodo-thyronine or thyroxine by way of di-iodotyrosine, although logical, had not been established biogenetically. The total iodine content of the thyroid gland is accounted for by thyroxine and di-iodotyrosine, both of which have been shown to occur abundantly in the thyroid gland. What accomplishes the coupling of di-iodotyrosine to form thyroxine? Insight into this mechanism was first clearly furnished by Ludwig and von Mutzenbecher,¹¹ who were able to iodinate casein, producing products whose physiologic activity was shown to be due to the formation of thyroxine. This remarkable synthesis has since lent itself to the inexpensive production of iodinated proteins of considerable physiologic potency that have been found useful in animal husbandry in increasing milk yield.^{12,13} Only two mechanisms are available to explain this formation of thyroxine: either the protein contained thyronine (thyroxine less all four of its iodine atoms), which directly added iodine to form thyroxine, or the iodine produced di-iodotyrosine from tyrosine and was then converted into thyroxine. Proof that the latter type of conversion could occur in minimal amounts was first adduced by von Mutzenbecher¹⁴ in 1939 and was shown by Harington and Pitt Rivers¹⁵ to depend on biologic oxidations. The final proof of the ability of thyroid tissue to convert di-iodotyrosine into thyroxine was furnished by tracer studies utilizing radio-iodine. This was accomplished by two methods. In the first, radioactive iodine was injected into animals and the distribution of radioactivity in the body subsequently determined; in the second, the respiration of thyroid-tissue slices was studied in a medium to which radioactive iodine had been added and whose fate could be traced.

Following the injection of radio-iodine into animals, there is rapid concentration of iodine in the thyroid gland.¹⁶⁻¹⁹ This occurs within a matter of minutes and proceeds until as much as 50 per cent of the radioactive material is found in the gland after forty-eight hours. The radioactive iodine is distributed among three fractions—morganic iodide, di-iodotyrosine and thyroxine—with increasing amounts of di-iodotyrosine and thyroxine with the passage of time. In fact, Morton and his co-

and a decrease in the pituitary gland. These investigators⁶⁴ state, "Thiourea and sulfadiazine, by depressing the formation of active thyroid principle, cause an increased release of thyrotrophin from the pituitary into the blood where, however, it appears in reduced amount because of its removal and increased utilization by the enlarging thyroid gland." Although the decreased amount of the thyroid-stimulating hormone found in the pituitary glands of the drug-treated animals is not explained, it has been shown by Albert et al.⁶⁵ that physiologically inactive amounts of these goitrogens augment the action of the thyroid-stimulating hormone when mixed with it *in vitro*. This synergism is also illustrated by the greater hyperplasia of the thyroid gland in animals treated with both thiouracil and thyrotropic hormone as compared with that in animals treated with either alone.

Whereas the goitrogenic action of the cyanides and probably of the cyanates could be inhibited by iodides, this was not found to be true with the thiourea derivatives,⁶⁶ which were in fact iodine-resistant goitrogens. But thyroxine or desiccated thyroid was early shown to prevent and abolish the goitrogenic and antithyroidal effect of these compounds as well as of the sulfonamides,³²⁻³³ indicating that they do not function by inhibiting the action of the thyroid hormone in the blood or peripheral tissues. Moreover, Malkiel⁶⁷ has found no destructive or inactivating effect of thiouracil and sulfaguanidine on endogenous circulating thyroxine.

The effect of the antithyroidal goitrogens on the metabolism of iodine has been explored by conventional techniques and through the use of radioactive isotopes of iodine. Thiouracil and sulfadiazine have been shown to cause nearly complete disappearance of iodine from the thyroid gland in five days.⁶⁸ This effect is inhibited by removal of the hypophysis or administration of thyroxine. Iodine reaccumulates after withdrawal of the drug, but this reaccumulation is retarded by hypophysectomy or the administration of thyroxine. The relation between the dose of thiouracil and thyroid weight and iodine content is quantitative enough to be used for the assay of new compounds.⁶⁸⁻⁶⁹

By studies of thyroid slices with radioactive iodine *in vitro*, Franklin and Chaikoff⁷⁰ found that the sulfonamides inhibited the formation of diiodotyrosine and thyroxine but did not alter the absorption of inorganic iodide from the surrounding medium. Thiouracil and thiocyanate were similarly shown by these investigators⁷¹ to depress or inhibit the formation of thyroxine and diiodotyrosine *in vitro*. They differed in their effect on iodine concentration by thyroid slices, however, thiouracil having little effect and thiocyanate causing marked depression of iodine uptake by the surviving tissues.

The inability of large amounts of iodine to overcome the stasis of hormone production caused

by thiourea was demonstrated in rabbits by Baumann, Metzger and Marine,⁶⁶ who showed that the drug caused rapid decrease in both thyroxine and nonthyroxine iodine in the gland itself, with excretion of the excess iodine in the urine. Further studies *in vivo* with radio-iodine have confirmed the result of the studies *in vitro* — namely, that thiouracil interferes in the living animal with the incorporation of iodine into thyroxine and diiodotyrosine in the thyroid gland⁷² and thus causes cessation of hormone synthesis.

Further details of the mechanism of action of thiouracil on iodine metabolism have been supplied by studies on the chick with radio-iodine. It was first demonstrated that thyrotropic hormone produces thyroid hypertrophy within twenty-four hours,⁷³ but no increased iodine uptake occurred until hyperplasia was marked. This accelerated uptake was not maintained with continued stimulation. In addition, thyrotropic hormone caused early and striking acceleration in the loss of radio-iodine from the gland, so that 75 per cent of the quantity initially stored was lost during the first day. This is interpreted as being due to "accelerated secretion of thyroid hormone from the gland induced by thyrotropic stimulation."

Next, a comparison was made of the effects of thiouracil and of thyrotropic hormone on the collection of radio-iodine and on the histology of the thyroid gland in the chick.⁷⁴⁻⁷⁵ The histologic changes produced were indistinguishable except for a lag of five days in the appearance of alterations caused by thiouracil. Within an hour after the injection of thiouracil, however, maximal inhibition of the uptake of radio-iodine occurred, with a gradual loss of this inhibitory effect over twenty-four hours. Following the withdrawal of thiouracil, the glands of the treated chicks collected radio-iodine in larger quantities than did those of the controls, in amounts similar to those collected by glands made hyperplastic with injections of thyroid-stimulating hormone. The inhibition of iodine collection resulting from thiouracil in the intact thyroid gland contrasts sharply with the *in vitro* studies previously described,⁷¹⁻⁷² but both sets of experiments confirm the hypothesis that thiouracil interferes with hormone synthesis by interfering with the metabolism of iodine. Thiouracil inhibited collection of radio-iodine by normal chick thyroid and by that made hyperplastic through thyroid-stimulating hormone and with thiouracil. Salter, Cortell and McKay⁷⁶ reached similar conclusions concerning the role of thiouracil — that it prevents the conversion of iodide to diiodotyrosine and thyroxine without, however, impeding the synthesis of uniodinated thyroid protein.

A more recent study by Chaikoff and his associates⁷⁷ has confirmed the depressing effect of potassium thiocyanate on the uptake of radio-iodine by thyroid tissue, either *in vitro* or in living animals.

increased thyroid activity caused by depressed oxygen consumption from the cyanide. Depressed oxygen utilization increased thyroid activity, goiter results if iodine is lacking in the face of added demands on the thyroid gland.

That the thiocyanates in addition to the cyanides exert a goitrogenic and antithyroidal effect was first observed by Barker^{38, 39} in hypertensive patients under treatment with potassium thiocyanate. Many similar cases subsequently reported have been reviewed by Estes and Keith⁴⁰. These goiters occur in about 4 per cent of such patients³⁹ and are characterized by thyroid hyperplasia, the signs and symptoms of myxedema, occasionally by exophthalmos and by an increased urinary excretion of inactivated thyrotropic hormone. Rawson and his co-workers^{41, 42} believe that the thiocyanate prevents the synthesis of thyroid hormone at some point distal to the uptake of iodine, since they were able to demonstrate excessive uptake of radioiodine by thiocyanate-induced goiters. Decreased hormone elaboration leads to hypometabolism and to stimulation of the anterior pituitary body, with excessive production of thyrotropic hormone. This causes thyroid hyperplasia without a corresponding increase in hormone output — "a hyperplasia of frustration." The administration of desiccated thyroid prevents or relieves thiocyanate goiter.

Thiocyanate therapy may also cause acute goiter clinically resembling thyroiditis⁴³ and pathologically showing extreme parenchymatous hypertrophy and hyperplasia⁴⁴ but without papillary infolding or lymphocytic infiltration. The colloid stains well, and the irregularity of the acini and a tendency toward invasiveness suggest neoplasia.

The antithyroidal and goitrogenic properties of the cyanides and cyanates were of experimental and toxicologic interest but failed of clinical application. In 1941, however, British and American investigators simultaneously revived interest in the chemotherapeutics of Graves's disease by parallel studies of new antithyroidal goitrogens. Kennedy and his co-workers⁴⁵ found that Brassica-seed diets produced large goiters in rats in spite of simultaneously administered iodide, the goiters required the presence of thyrotropic hormone for development or maintenance, since they did not develop in hypophysectomized animals and regressed after hypophysectomy^{46, 47}. The active goitrogenic principle was demonstrated to be thiourea or allyl thiourea⁴⁸.

Meanwhile, Richter and Clisby,⁴⁹ in searching for an improved rat poison, discovered that phenyl thiourea caused marked hyperplasia of the thyroid gland. Somewhat earlier, the MacKenzies and McCollum⁵⁰ found that sulfaguanidine caused marked thyroid hyperplasia.

In this initial phase of study, chief emphasis had been placed on goitrogenesis — an iteration of the early work with the cyanides and cyanates. Astwood and others⁵¹ and simultaneously the Mac-

Kenzies⁵² directed attention to the more important effect of these compounds as inhibitors of thyroid function. Both groups of investigators first studied the sulfonamides and thiourea, finding the latter many times more effective than the former as an antithyroidal drug. Both caused thyroid hypofunction, with reduced oxygen consumption and impairment in growth and development. The thyroid glands were enlarged, hyperemic and hyperplastic, with decreased colloid and increased acinar-cell height. Papillary infoldings of the epithelium were frequently observed. Omission of the drugs was followed by histologic and physiologic return to normal.

The shifting of emphasis from goitrogenesis to antithyroidal activity was followed by widespread research into the compounds that maximally depressed thyroid function and were only incidentally productive of thyroid enlargement. Thiourea, thiouracil and their derivatives were found to be the most potent compounds for inhibiting thyroid function⁵³. In a more recent study of over two hundred and twenty substances, Astwood, Bissell and Hughes⁵⁴ found two types of chemical structure associated with antithyroidal activity. The more active substances were derivatives of thiouracil and possessed a thiocarbonamide grouping, the less active substances possessed an aminobenzene group, such as the sulfonamides, and were a fourth as active as thiouracil. The most active of the former group proved to be 6-N-propyl thiouracil.

To this "periodic table" of antithyroidal goitrogens established by Astwood, other investigators⁵⁵⁻⁶¹ added and undoubtedly will continue to add various active compounds, since the slightest shift in chemical structure or linkage produces marked pharmacologic differences.

The morphologic and physiologic effects of these compounds, particularly thiouracil, have been abundantly studied so that an accurate postulation of the mechanism of hormone inhibition can be constructed. Thiouracil retards growth, induces cretinism in newborn rats and antagonizes the effects of injection of the growth hormone of the anterior pituitary body^{62, 63}. The presence of the pituitary is essential for the production of goiter with these drugs,^{48, 61, 62} since no thyroid hyperplasia occurs in hypophysectomized animals following their administration, in fact, the thyroid gland regresses as in untreated hypophysectomized animals. The goitrogenic effect results from pituitary stimulation and not from direct action by these compounds on the thyroid parenchyma.

No increase of thyrotropic hormone is demonstrable in the blood or hypophysis of rats treated with thiourea or sulfadiazine, in fact, there is a decrease as compared with marked increases found in thyroidectomized animals⁶⁴. Animals pretreated with thiourea and then thyroidectomized showed an increase of thyrotropic hormone in the blood.

so-called "chemical thyroidectomy" and in the preoperative preparation of patients for thyroidectomy, either alone or in association with iodides

When thiouracil was used as the sole agent in the treatment of Graves's disease, about 50 per cent of patients remained in remission and the other 50 per cent relapsed within two weeks to five months⁸⁴⁻⁸⁶. In general, patients treated for nine to twelve months had a smaller relapse rate than those treated for shorter periods, but Williams⁸⁶ obtained remissions lasting as long as twenty months in several patients who were under treatment for only two months. On the other hand, relapses occurred in several patients who had been treated for as long as twenty months. Lasting remissions occurred more frequently in female patients with small glands and mild hyperthyroidism.

The use of thiouracil in the preparation of the patient for thyroidectomy has been extensively reported⁸⁴⁻⁸⁶ and has established itself as the agent of choice for severe cases of thyrotoxicosis because it almost invariably reduces the metabolism to normal and renders a one-stage thyroidectomy feasible in patients who previously required multiple operations. When thiouracil is used as the sole drug, however, the gland is so vascular and friable that hemostasis is arduous and the gland more difficult to handle. Fortunately, the addition of iodides in the preoperative preparation, either in conjunction with thiouracil or for a period of seven to fourteen days preceding the operation, greatly reduces the vascularity and allows adequate control of bleeding at operation. In our experience the two drugs may be used simultaneously up to operation, since thiouracil and its derivatives do not repress the involuting effect of iodine on the hyperthyroid gland^{85, 89, 97}.

During the early experience with thiouracil in the treatment of toxic goiter, it appeared that preliminary administration of iodide slowed the rate of improvement, and it was believed that this was due to the effect of iodine in causing increased hormone storage. More extensive experience has shown that there is considerable variation in the effect of iodide on subsequent thiouracil therapy in Graves's disease,^{84, 87} and this has been our experience. In rats simultaneous administration of sodium iodide and methyl thiouracil resulted in the typical iodide effect — flattening of the epithelium and colloid accumulation. The same investigator⁸⁸ found greater inhibition of thyroid function when both substances were administered to thyrotoxic patients than with either alone, and concludes that no specific antagonism between the effects of goitrogenic substances and iodine is apparent, iodine and the thyrotropic hormone or the goitrogens must be supposed to have different points of attack, since the two phases can be accelerated co-ordinately. Danowski, Man and Winkler⁸⁹ also found that previously administered iodine did not significantly interfere with the subsequent antithyroidal effect of thiourea.

The inter-relation between thiouracil and iodine as they affect the hyperplastic gland in Graves's disease has led to a reformulation of the mode of action of iodine in this disease by the Thyroid Clinic of the Massachusetts General Hospital¹⁰⁰. The function of iodine in supplying an essential ingredient for thyroid economy is termed its "iodinating action," which may be served by as little as 0.075 mg of iodine daily. In Graves's disease the rapid manufacture of thyroid hormone creates an iodine uptake by the gland two or three times that in normal persons. The administration of iodine in daily doses of 60 mg or more meets the demands of increased hormone production and thus induces regression of the gland toward normal — the so-called "involuting action" of iodine. Under thiouracil treatment the hyperplastic gland in Graves's disease becomes more hyperplastic. In spite of the fact that thiouracil prevents the utilization of iodine for hormone synthesis, the iodine causes involution of the thyroid gland in Graves's disease. Therefore, it is concluded that iodine exerts an iodinating and an involuting action on the gland in Graves's disease and that these two actions can be separated by means of thiouracil.

Toxic Reactions

Early observations quickly showed the varied toxicity of thiourea and thiouracil. The principal toxic reactions comprised the following dermatitis, drug fever, swelling of the submaxillary glands, leukopenia and agranulocytosis. Less frequent reactions are the following: edema of the legs, purpura, hematuria, Mikulicz's syndrome, pericarditis, periarteritis nodosa and psychosis. These reactions have been described and reviewed extensively¹⁰¹⁻¹⁰³. In addition, they have been the subject of co-operative studies covering 1091 patients in one group¹⁰⁹ and 5745 in another¹¹⁰. It is clear from these analyses of the toxic manifestations in large groups of cases that approximately 15 per cent of all patients will show some type of adverse reaction to thiouracil. All the principal reactions promptly disappear on omission of the drug except agranulocytosis, which is the most serious complication of thiourea and thiouracil therapy and requires special consideration because of its frequently fatal issue. It occurs in about 2.5 per cent of cases, with a varying fatality rate of 15 to 25 per cent and an overall mortality in large series that is constant at 0.4 to 0.5 per cent. Agranulocytosis tends to occur in the early weeks of treatment, but no general rule can be laid down that will guarantee freedom from serious hematologic reactions. As Lesses and Gargill¹⁰⁶ state

Dosage, duration of treatment, constant or intermittent therapy, associated clinical phenomena and premonitory symptoms have not proved safe guides. Serious reactions have occurred at both high and low dosage levels, with short and with long treatment and with both constant and intermittent administration of the drug.

maintained on an iodine-poor diet. Following the disappearance of potassium thiocyanate from the circulation, the whole gland does have an increased uptake of radio-iodine, but this increase is not apparent when expressed in terms of unit weight of tissue. Thus, the drug does interfere with the removal of iodine from the circulation when iodine is not readily available in the diet. It also inhibits conversion of inorganic iodide to di-iodotyrosine and thyroxine, as shown by low thyroxine content of the gland and decreased levels of protein-bound iodine in the blood. VanderLaan and Bissell⁷⁸ have likewise confirmed this course of events by showing that rats fed propyl thiouracil readily take up radio-iodine in their thyroid glands but retain it only for a short time, possibly because it is not hormone-bound, and that in the presence of both propyl thiouracil and potassium thiocyanate there is delayed and only moderate iodine uptake by the gland. They conclude that "in the presence of thiocyanate the ability of the thyroid gland depleted of iodine to take up injected iodine is considerably impaired." These recent studies indicate the importance of time relations in the study of the influence of goitrogens on iodine uptake.

The evidence that the biosynthesis of thyroxine is intracellular, aerobic and enzymatic has been discussed above. The iodination of tyrosine to di-iodotyrosine requires liberation of iodine from iodide. The formation of di-iodotyrosine and thyroxine is "linked with aerobic oxidations involving the cytochrome-cytochrome oxidase system."⁷⁴ The effect of the sulfonamides and thiouracil on this enzyme system is controversial, Franklin and Chaikoff⁷⁰ observing no effect with the sulfonamides and Dempsey⁷⁵ noting that thiouracil readily inhibited the peroxidase reaction in thyroid tissue but did not affect the cytochrome oxidase reaction. McShan, Meyer and Johansson⁷⁹ found no inhibition of cytochrome oxidase or of succinoxidase in thyroid tissue by sulfonamides and thiouracil. On the other hand, Paschkis and his co-workers⁸⁰ report that thiouracil and the sulfonamides inhibit the cytochrome oxidase *in vitro* as well as in the thyroid gland itself. Bevelander,⁸¹ after studies on sea-urchin egg development, concluded that thiourea acts by inhibition of enzyme systems necessary for the growth of the sea urchin. Tipton and Nixon⁸² observed significant depression of succinoxidase and cytochrome oxidase in the liver of rats.

Thiouracil acts by preventing iodination and hormone synthesis, but it is still not clear whether it acts as an antioxidant, through depression of the enzyme systems or by some mechanism other than that of inhibition of oxidation.

THIOURACIL AND RELATED COMPOUNDS

Clinical Use

Since Astwood⁸³ first used thiourea and thiouracil in the treatment of hyperthyroidism, numerous re-

ports have appeared dealing with many thousand of cases. The experience with thiouracil is extensive, but its toxicity has led to clinical studies with other derivatives and related compounds. Excellent reviews concerning large series of cases treated with thiouracil for long periods have been published by Astwood,⁸⁴ Barr and Shorr⁸⁵ and Williams.⁸⁶

The anatomic effects produced in the human thyroid gland by thiouracil have been chiefly studied in the hyperplastic gland of Graves's disease. The size of the gland may increase, decrease or remain unaltered, but the gross increases in human beings have not been so striking or so constant as those in experimental animals. Prolonged treatment has usually resulted in a decrease of the gland⁸⁷ unless myxedema supervenes. Histologically, however, there is great similarity to the experimental effect with increased thyroid hyperplasia, loss of colloid and increased vascularity.^{88, 89} Changes in the pituitary gland similar to those found in animals—increased basophilism and absent eosinophilism—have been reported.⁹⁰

Physiologically, thiouracil decreases the basal metabolic rate, frequently at the same rate as iodine,^{84, 88} and in many cases causes clinical myxedema if continued for several months.^{84, 85} Myxedema, however, has not yet been conclusively produced by thiouracil in persons with normal thyroid function,⁸⁴ the normal economy evidently possessing adequate homeostatic mechanisms for resisting the usual goitrogenic and thyroid-depressing effects of this compound. Following the administration of thiouracil in Graves's disease, the uptake of tracer doses of radio-iodine is greatly diminished with an increased urinary excretion,⁸⁸ as previously described in animal studies. The hormonal iodine of the blood returns to normal,⁹¹ the blood cholesterol rises,⁹² the calcium, phosphorus and protein balances become more positive and creatinuria decreases.⁹³ In general the physiologic effects produced are such as would occur with amelioration of thyrotoxicosis and a return to the euthyroid state. These changes, which occur far more regularly than with iodine therapy, may take from several weeks to several months for completion.

The effective dosage of thiouracil for initial therapy is generally 0.6 gm daily, in doses of 0.1 gm at regularly spaced intervals. The dosage is reduced as the basal metabolic rate approaches normal, and maintenance doses of 0.05 to 0.2 gm are utilized for long periods. Intermittency of treatment is avoided, since it is considered to be a contributing factor in toxic reactions. Subjective and objective clinical improvement usually appears within seven to ten days after the initiation of therapy. The basal metabolic rate and blood-cholesterol levels serve as adequate laboratory guides in the regulation of dosage.

Thiouracil has been used in two ways as the sole agent in the control of thyrotoxicosis to produce a

Recent progress reports by Hertz and Roberts¹²³ and by Chapman and Evans¹²⁴ deal with the use of radioactive iodine in a total of 51 cases followed up to five years, the former continuing to advocate supplementary iodide therapy following the ingestion of radio-iodine but the latter finding it unnecessary.

Radioactive iodine is prepared in a cyclotron by nuclear bombardment of metallic tellurium that becomes transmuted into iodine. This must be dissolved, distilled and reduced to sodium iodide. The final product as administered is dissolved in distilled water to contain 14 to 79 mc of twelve-hour iodine. This is ingested by the patient within one to four hours after conclusion of the bombardment. The dosage given is dependent on the estimated weight of the thyroid gland, about 0.5 to 1 mc of twelve-hour iodine per gram of thyroid being utilized, in doses ranging from 5 to 25 mc in one series¹²³ and an average of 40 to 50 mc in the other.¹²⁴ Large doses may cause radiation sickness. Ordinary iodine therapy should be withheld for several weeks before the administration of radio-iodine, to ensure adequate concentration of the radio-iodine by the thyroid gland. Biopsies indicate that radio-iodine causes fibrosis of the gland similar to that seen with external irradiation. Adequate doses, either single or multiple, have caused sustained remissions in about 80 per cent of the patients treated. Personal observations in a small number of cases indicate that single doses ranging from 8 to 25 mc were frequently ineffective in producing a remission and required supplemental use of iodides.

More data must be accumulated before final judgment can be made of the place of radio-iodine in the therapy of Graves's disease, particularly regarding the undesirable late effects from the "internal radiation." On a theoretical basis the administration of radioactive iodine seems unlikely to produce deleterious late effects. The beta rays emitted have a maximum range of a few millimeters of tissue, and whatever radio-iodine is not absorbed by the thyroid gland is excreted in the urine.

BLOOD-IODINE STUDIES

Determination of the blood-iodine level has become increasingly important in the diagnosis and management of thyroid disease. The concentration of precipitable or protein-bound iodine in the serum is probably an index of the amount of circulating thyroid hormone and hence is also called "hormonal iodine." The methods, which are relatively exact but arduous, require considerable skill in the techniques of analytical chemistry, so that they are not suitable for routine clinical laboratories. The information obtained, however, is sufficiently valuable to warrant greater clinical use.

Curtis^{125, 126} has recently reviewed a large experience extending over thirteen years utilizing whole-blood-iodine levels rather than those of precipitable serum iodine. In toxic goiter, whether diffuse or nodular, the level of blood iodine was consistently elevated to about twice normal (4 microgm per 100 cc as contrasted with 8 microgm per 100 cc). In his final conclusion, however, he states "The determination of the basal metabolic rate is a more reliable test of thyroid activity than the level of the unfractionated whole blood iodine. However, both determinations, considered together, are superior to either alone."

Winkler and his collaborators have contributed important studies on the precipitable serum iodine in hypothyroidism¹²⁷ and hyperthyroidism¹²⁸ and on the effect of ingested desiccated thyroid in subjects with normal thyroid function.¹²⁹ In untreated myxedema the serum iodine was characteristically subnormal or absent, treatment with thyroid caused a linear elevation in the level of serum iodine in accordance with the dosage of thyroid, 0.07 gm (1 gr) elevating the serum iodine by 2 microgm per 100 cc. The basal metabolic rate responded more slowly than the iodine levels to alteration in the thyroid state.

In hyperthyroidism at least 95 per cent of all cases had elevation of the precipitable serum iodine. This elevation frequently declined with administration of iodides — occasionally to normal levels — and was restored to normal or subnormal levels following radical subtotal thyroidectomy. Low values frequently persisted permanently, associated with normal metabolic rates but with slight elevations in the serum cholesterol and some clinical evidence of mild hypothyroidism. The level of the serum iodine, therefore, appeared to be more sensitive than the basal metabolic rate in measuring thyroid hypofunction.

When desiccated thyroid was administered to normal subjects there was far less change in the metabolic rate and serum iodine than in myxedema. The administration of 0.7 to 2.0 gm (10 to 30 gr) of dried thyroid, however, caused abnormally high serum iodine, an elevated basal metabolic rate and clinical signs of thyrotoxicosis. Although the normal subject was resistant to thyroid, once enough was given to raise the serum iodine, the correlation between rises in that value and the basal metabolic rate was exactly the same as that in myxedematous patients. Two conclusions were drawn from this study: normal tissues are as sensitive to thyroid as myxedematous and the degradation of normal iodine to inorganic iodine by the normal thyroid gland probably explains the tolerance of euthyroid subjects to large doses of thyroid. This paper contains several instructive graphs showing the parallelism between precipitable serum iodine and basal metabolic rate when thyroid is administered.

Because no protective treatment is available, frequent observation of the patient receiving thiouracil is essential, and white-cell counts should be done three times a week, with estimation of the neutrophil percentage whenever the total white-cell count is below 5000. The patient should be cautioned to report promptly the development of fever, dermatitis or sore throat. If severe neutropenia or agranulocytosis develops, the drug should be promptly omitted and vigorous therapy with penicillin and transfusions should be started.

The unpredictable occurrence of agranulocytosis with thiouracil therapy must be balanced against the risks of thyroidectomy. Since many of these risks are caused by the inability of iodine to induce an optimal remission, the use of thiouracil offers an opportunity to avoid the mortality associated with surgery in severely toxic cases. Although the risks of thyroidectomy are greatest in patients with severe thyrotoxicosis or with associated cardiovascular disease, a fatal reaction to thiouracil may occur in mild or uncomplicated cases. For this reason, thiouracil is best employed as a preoperative agent along with iodine in patients who are severely toxic. The mildly toxic group is best managed with iodine followed by thiouracil and thyroidectomy if iodine alone fails to induce and maintain a complete remission. Thiouracil also has a proper place in the treatment of patients who refuse operation or who are unable to have surgery because of coincidental serious disease or when adequate surgical facilities are not available. Patients with toxic nodular goiters and a small group with exceptionally large diffuse toxic goiters should be subjected to thyroidectomy after preparation with either iodine alone or with thiouracil and iodine, depending on the degree of toxicity. Thyroidectomy is eventually indicated in this group, either because of pressure effects or because of possible neoplastic disease in the nodular goiters.

Continuous therapy with thiouracil, if essayed, should be restricted to patients who can be closely observed and whose temperament and occupation readily lend themselves to such observation. Another hazard of continuous thiouracil therapy is the possibility that it will stimulate carcinogenesis in the thyroid gland. Thiourea, when administered to rats together with the carcinogen acetaminofluorene, produces rapidly growing tumors, which neither alone evokes.¹¹¹ Paschkis and his associates¹¹² found that thiouracil induces mitosis stimulation in rats kept at low temperatures, as measured by the colchicine technic.

The toxic manifestations of thiouracil have led to clinical trials of many related compounds in an effort to circumvent the undesirable side effects. Thiobarbital,¹¹³⁻¹¹⁵ methyl thiouracil,¹¹⁶⁻¹¹⁹ amino thiazole,¹²⁰ 6-N-propyl thiouracil^{121, 122} and many others have been utilized.^{97, 123} The first three proved at least as toxic as thiouracil. Amino thia-

zole is still under study. Propyl thiouracil in preliminary clinical studies produced only urticaria dermatitis but was highly toxic to rats,¹²⁴ so that no final estimation of its toxic potentialities can be made at present. Sensitization phenomena appear to be frequently linked with the toxic qualities of all these compounds.¹⁰¹⁻¹⁰⁵

OTHER ANTITHYROIDAL AGENTS

The effectiveness of the antithyroidal goitrogen depends on their interference with the production of thyroid hormone. They do not in themselves antagonize or neutralize the effect of circulating thyroxine so that they are antithyroidal by indirect rather than specifically. Recently, certain compounds have been claimed to be particularly antagonistic to thyroxine itself. Carter and his collaborators¹²⁵ found a substance in ox and whale liver and in human urine—identified as paraxanthine (1, 7-dimethylxanthine)—that was capable of converting the temperature-heart-rate curve of the summer frogs' heart into the curve of the winter frogs' heart. This substance, which was isolated in crystalline form, appeared to counteract the effect of thyroxine in rats. Barker¹²⁶ and Williams,¹²⁷ however, were unable to find significant antithyroidal action from this drug as measured by effects either on oxygen consumption or on tadpole metamorphosis. It had no observable result when given to a thyrotoxic patient for a period of eleven days.

Mansfeld¹²⁸ extracted from the thyroid gland and human serums crystalline substances called "thyrothyryl A and B" that are capable of producing as much as a 50 per cent lowering of oxygen consumption in rats. This work has not yet been confirmed but the compounds involved may be related to certain structural analogues antagonistic to thyroxine investigated by Woolley.¹²⁹ These were newly synthesized ethers of N-acetyl di-iodotyrosine that did counteract the pharmacologic effects of thyroxine on tadpoles but that, in the absence of thyroxine, were chemically close enough to it to have a slight thyroxinelike effect themselves. This development may hold promise for eventual isolation of a natural antithyroidal compound without the toxic complications of the thiourea derivatives.

RADIOACTIVE IODINE

In 1938 Hertz, Roberts and Evans¹⁶ introduced radioactive iodine as an aid in the study of thyroid physiology. The hyperthyroid gland was found to absorb as much as 80 per cent of small tracer doses of radio-iodine.¹³⁰ Its application to the treatment of Graves's disease by Hertz and Roberts¹³¹ and by Hamilton and Lawrence¹³² quickly followed. The latter authors reported 3 cases of hyperthyroidism that were completely remitted after adequate doses of radio-iodine. In the former series ordinary iodides were given in addition to the radio-iodine.

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EXOPHTHALMOS IN THYROID DISEASE

The problem of exophthalmos associated with toxic goiter has continued to excite the interest of investigators and to harass and mystify the clinician. Two exhaustive reviews, dealing particularly with the clinical problems, have recently appeared by Mulvany¹⁴⁰ and Woods,¹⁴¹ whereas the experimental aspects have been most instructively studied by Albert.¹⁴² Woods summarized the present status of the subject as follows:

A critical review of all the various theories and experiments in the etiology of the exophthalmos of primary toxic goiter permits but one conclusion—the problem is still unsolved. The evidence indicates that exophthalmos is probably not related to a thyrotoxicosis and not related at all to a sympathicotonia. The weight of evidence would indicate that both the thyrotoxicosis and the exophthalmos are related in some way to the action of an anterior pituitary hormone or several hormones. Any effect by thyroxine appears to influence favorably the exophthalmos. Deficiency in the gonads or adrenal cortex may play a considerable role in the picture.

If the exophthalmos is in truth initiated by an anterior pituitary hormone, the means by which it accomplished this end is still a mystery. The anatomical evidence all points strongly to the impossibility of the eye being pushed or pulled forward by any muscular action. Edema and hypertrophy of the orbital contents with some inflammatory reaction is present but whether this is primary or secondary is undetermined. Once initiated, however, the orbital hyperplasia may continue or persist despite the control of the metabolic phases of the disease.

There is considerable clinical evidence that any measure that quickly and completely alleviates the thyrotoxicosis may worsen the hyperophthalmia of patients with severe or malignant exophthalmos.¹⁴³⁻¹⁴⁶ Although this is not invariable, its occurrence is frequent enough so that in thyrotoxic patients with severe ophthalmopathy the effect of any therapy on the eyes should be given first consideration. Ordinarily this would call for gradual control of the thyrotoxicosis, such as with external irradiation, chemical thyroidectomy with thiouracil or iodide or radioactive iodine therapy.¹⁴⁷ A remission induced with radioactive iodine in 1 case did not increase severe exophthalmos.¹³⁴ Thyroid administration is perhaps helpful and should be utilized to the point of tolerance for long periods as soon as the intrinsic thyrotoxicosis is brought under control. The work of Winkler¹³⁷⁻¹³⁹ suggests the desirability of administering enough thyroid to raise the serum iodine to thyrotoxic levels. The determination of the basal metabolic rate can be used as an indirect guide to the level of hormonal iodine if facilities for the latter estimation are not available.

Experimentally Albert¹⁴² has conclusively demonstrated that the anterior pituitary gland contains an exophthalmogenic factor that produces striking exophthalmos in the fundulus—the common Atlantic minnow. This factor parallels the thyroid-stimulating hormone of the pituitary gland both qualitatively and quantitatively and may be that

hormone or one closely related. In the fundulus the exophthalmos is due to secretion of fluid by the orbital tissues into the retrobulbar space. The fluid presses the eyeball forward and thrusts it out of the orbit by overcoming the pull of the extraocular muscles. Albert's work holds definite promise for the future elucidation of the clinical problem of exophthalmos.

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slightly movable and did not seem to be attached to the cervix. The fundus was not palpable. The mass was also felt on rectal examination.

The temperature was 101°F, the pulse 96, and the respirations 22. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 8600, which rose to 10,800 on the fourth hospital day. The urine and stools were normal. X-ray examination revealed a questionable soft-tissue mass represented by an 11-cm. area of decreased density in the pelvis. The cervical discharge was negative for streptococci and gonococci but abundant beta-hemolytic streptococci were cultured from the urine.

In the hospital the temperature remained between 99 and 100°F. On the fourth day the fundus of the uterus was felt anteriorly to the left of the midline, and an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. CARROLL MILLER. We have here the record of a young woman — apparently in good health, without previous disease or surgery — who was seized with a sudden abdominal pain whose nature makes one think that it was dependent on an acute abdominal condition. The disease must have been in the lower abdomen, and we should consider three systems in formulating a differential diagnosis. The urinary tract can be dismissed quickly because of the lack of urinary symptoms. It is true that the patient had urinary frequency, but she had no dysuria in the hospital. Beta-hemolytic streptococci were cultured from the urine. It has been found not infrequently that pathologic conditions in the kidney, the ureter and the bladder may produce a picture simulating an acute abdominal emergency. Pyelitis or ureteral stone will cause pain, spasm, nausea and vomiting, an urge to urinate at frequent intervals and sometimes dysuria. The symptoms that this patient presented, however, do not suggest to me either pyelitis or stone, and the microscopic examination of the urine seemed to rule these out after admission.

The gastrointestinal tract, particularly the small and large bowel, should next be considered. In any acute abdominal condition one first suspects appendicitis. Symptoms of appendicitis are unusual on the left side of the abdomen. There may be a malrotation of the colon, with the cecum and appendix on the left of the midline, some information may be obtained from the x-ray film about the position of the colon, even though a barium enema was not done. The progress of the symptoms suggests a sudden rupture or extension of a long-standing process in the lower abdomen that was not, however, sufficiently virulent to cause peritonitis. In cases of ruptured appendix or a ruptured Meckel's diverticulum, one finds evidence of persistent and

usually widespread peritoneal infection and inflammation. We should always think of sigmoidal diverticulitis in cases of sudden left-sided lower abdominal pain, but it is rare to have diverticulitis in a person in the early decades of life — this patient was thirty years old, and the usual symptoms occur after forty. It is quite possible that a rupture of an infected diverticulum caused a peritoneal reaction at first, which became walled off, with the formation of an abscess. Again, I think that we can rule out rupture of a carcinoma of the sigmoid or rectum because this patient apparently had had no previous bowel disturbance. Examination of the stools was negative for blood, I assume, and she did not present a history of carcinoma, either from obstruction or from other interference with bowel habits. A volvulus of the sigmoid is something that we see fairly often. This may produce rather low-grade obstruction, which becomes more marked as time goes on. It may cause marked peritoneal irritation as the circulation in the twisted loop becomes impaired. It is unlikely, however, that this patient would have recovered from the condition so easily and so well as she apparently did. The confusing finding that turned up later in the illness is the mass in the right side of the pelvis, when the original pain was experienced on the left.

So far as the internal female genitalia are concerned, I think that we must consider first and always the possibility of extrauterine pregnancy. We cannot always depend on the menstrual history in cases of pregnancy because we have all seen patients two, three or four months' pregnant who have had some flow at the usual menstrual time. We assume that this last period, twelve days before the pain started, was a normal one. The patient was obviously an obese woman, and examination of the abdomen was undoubtedly difficult. She may have had pelvic inflammatory disease, with hydrosalpinx, or diffuse ovarian pseudomucinous cysts. She may have had a simple ovarian cyst that was not large enough to cause symptoms of pressure or pain prior to the onset of the present illness. This may have become twisted during the night before she was awakened with pain, and with increasing infarction it may have ruptured. I should like to believe that this process was primarily a rupture of a small hollow viscus or cyst, with flooding of the peritoneal cavity and with gradual subsidence of the diffuse peritoneal reaction and residual fluid into an abscessed mass. Let us not call it an abscess but encapsulated fluid. I should be interested to know what the hemoglobin determination was when she was examined in the hospital.

DR. TRACY B. MALLORY. The hemoglobin determination is not recorded.

DR. MILLER. I think that we should all like to know what the hemoglobin was, because if there was blood in the abdomen there should have been a fairly moderate reduction in the hemoglobin.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32461

PRESENTATION OF CASE

A thirty-one-year-old housewife entered the hospital because of lower abdominal pain.

At 5:00 a.m., eight days before admission, the patient was awakened by a sharp pain in the left lower quadrant, flank and thigh. It was intermittent and severe enough to make her cry out. She desired to move her bowels, but could not. The pain persisted all day, without anorexia, nausea or vomiting. Two enemas were administered. Since only a small portion of the fluid was evacuated, the patient swallowed three tablespoonfuls of milk of magnesia. On the following day the pain spread over the entire abdomen and was constant. A physician prescribed "white pills," fluids and bed rest because of

fever. Six days before admission a soapsuds enema initiated a diarrhea that lasted four days. The stools were loose and yellow. The patient felt more feverish, and the abdomen appeared distended. The pain was persistent, but less severe. On the following day she began to have severe cramps over the entire abdomen. Anorexia was marked. The patient lasted until two days before admission, when the patient began a soft diet, the diarrhea eased, and the pain was less severe. On the day before admission the physician advised hospitalization because of continued fever. By the time of admission the pain was reduced to a dull ache in the left flank and over the symphysis. During this illness there was some urinary frequency but no dysuria.

The patient had had three children, the last one a year before entry. The menses had been normal. The last period had begun twelve days before admission and had lasted three days. Four years before admission she had had a post-partum phlebitis for which bilateral ligations were performed. For several years varicose veins had caused some pain on standing, and several had been injected.

On physical examination the patient did not appear ill. She weighed 240 pounds. There was diffuse tenderness throughout the lower abdomen without spasm or rebound tenderness. There was a slight white discharge from the cervix. Motion of the cervix did not cause pain. There was slight tenderness in both vaults, and a large, firm mass was palpated in the right vault that was

ventricle was enlarged, and there were areas of focal collapse in both lower lung fields. An electrocardiogram showed a PR interval of 0.21, with a rate of 100. There was moderate left-axis deviation. A second electrocardiogram six days later was normal. The sedimentation rate at intervals of fifteen minutes was 6, 30, 43 and 46 mm. The blood Hinton reaction was negative.

The temperature rose to 100 to 100.5°F daily. After seven days the patient's condition was unchanged, and she was discharged.

Final admission (eleven days later). After discharge the symptoms were approximately the same as previously until the night before admission, when the patient suddenly experienced a smothering sensation and had difficulty in breathing. This was followed by much coughing productive of white phlegm.

On physical examination there was moderate respiratory distress, with many coarse crackling rales all over the lung fields. The neck veins were engorged, and the liver was palpable. The coughing was accentuated by motion. The heart rate was 130. The respirations were 30. The blood pressure was 132 systolic, 90 diastolic.

Five minutes later the severe dyspnea had disappeared, and the rales were remarkably reduced. During the next twenty-four hours there were two attacks of dyspnea with venous engorgement and rales. Treatment included a total of 24 mg. of morphine, aminophyllin, oxygen and tourniquets. At the end of twenty-four hours the respirations were 9 per minute, the blood pressure was 90 systolic, 62 diastolic. There were a few basal rales bilaterally. The patient died shortly afterward.

DIFFERENTIAL DIAGNOSIS

DR. CONGER WILLIAMS. I think that it would be well to rearrange the symptoms in the order of their appearance and try to decide what this woman had at the time of admission. First of all, for twenty years she had had an insidiously developing productive cough that was worse during the afternoon. Whether that was related to the terminal episodes, I cannot say, it may have been chronic bronchitis, even of slight degree, or chronic irritation from pressure on a bronchus, although I think that that is less likely. Seven years before admission the patient became dyspneic and gained weight. X-ray studies showed an enlargement of the heart. We might consider some sort of underlying heart disease at that time, but the etiology is not clear in the absence of a history of hypertension or findings suggesting significant valvular disease. It might be that the heart had been enlarged from some underlying chronic heart disease but that the patient at the same time had dyspnea from another cause. Dyspnea from heart disease that clears up for seven years on digitalis alone is rather unusual. It is

also possible that she had mild heart disease to begin with, exaggerated by some other complication such as infection or auricular fibrillation, although it is impossible to say which at this point. For five years before admission she had a dull ache throughout the chest, which apparently was constant and was not related to breathing. Constant chest pain, which is unusual and often implies some pressure phenomenon, is a fairly frequent symptom of expanding aortic aneurysm, but is almost unheard of as a symptom of coronary disease over such a long period. Other possible causes of chest pain, constantly present for five years, are few. It is unlikely that an expanding tumor in the mediastinum produced pain in the chest for so long.

Two other symptoms might be considered together. It is stated that the patient stopped giving long lectures because they made her hoarse, I suppose that she was hoarse at other times also. Four years before admission she raised blood-streaked sputum, and it is possible that these two symptoms were related. She may have had a local lesion in the larynx that produced bloody sputum and hoarseness, but I think that that is unlikely. A local malignant tumor of the vocal cords should not persist that long without further complications. Tuberculosis of the larynx might produce blood spitting and hoarseness but is usually associated with widespread pulmonary tuberculosis. I think it likelier that these two symptoms were caused by something lying outside the larynx, probably something in the mediastinum, which not only produced hoarseness by recurrent laryngeal-nerve paralysis but also bleeding by pressure on the bronchial tree.

Another symptom accompanying the constant pain in the chest was described as exertional dyspnea. Whether that was cardiac in origin or related to extrinsic pressure on the bronchial tree, I cannot say at this point.

The next development of importance occurred the day before hospital admission, when after walking half a block the patient felt as if the chest were being squeezed. She also felt as if something were expanding in the chest, which may indeed have been the case. At the same time she was dyspneic and weak and had difficulty in talking. The pain of coronary insufficiency, whether from angina pectoris or from acute thrombosis, is often described as a squeezing or an expanding pain. It is quite possible that this pain that occurred on the day before admission was on a coronary basis. We are not told how long it lasted. Is it known whether it was a matter of a few minutes or hours?

DR. EDWARD BLAND. The pain lasted all day, from 9.30 in the morning. In the afternoon, when Dr. Davenport saw the patient, she was still having pain, but it was less severe.

DR. WILLIAMS. I think that a blood-pressure difference of 20 points systolic between the two arms

It is quite possible that an extrauterine pregnancy did rupture. The peritoneal irritation was caused by either blood or cystic fluid and accounted for the nausea, the distention, the fever and the urge to move the bowels at first and the diarrhea later. Of course, the magnesia would have influenced the bowel habits. At any rate, there seems to have been some resolution of the process as time went on, so that the mass finally became definitely palpable and the fundus of the uterus could easily be outlined and was found to be pushed over to the left side. There was no question at that time of the location of the mass.

May we see the x-ray films that show the area of decreased density?

DR. MILFORD D. SCHULZ: This film shows the area of density in the pelvis. We should pay particular attention to that. The observer used the term "decreased" density. If that is true, it might be a cyst containing fatty material.

DR. MILLER: It is not delineated enough to call it a loop of bowel with air in it?

DR. SCHULZ: There is no indication that it is a dilated loop of small bowel.

DR. MILLER: I do not get much help from the x-ray film. I should guess that this patient had a ruptured ovarian cyst, with persistent bleeding and subsequent formation of a residual mass. My second choice is a ruptured tubal or extrauterine pregnancy.

CLINICAL DIAGNOSIS

Ovarian cyst
Pelvic abscess?

DR. MILLER'S DIAGNOSIS

Ruptured ovarian cyst, with hemoperitoneum and hematoma of adnexa

ANATOMICAL DIAGNOSIS

Dermoid cyst of left ovary, with twisted pedicle.

PATHOLOGICAL DISCUSSION

DR. MALLORY: When the abdomen was opened a moderate amount of orange-colored fluid was seen free in the peritoneal cavity. As exploration was continued a large mass was found adherent to the posterior surface of the uterus impacted in the posterior cul-de-sac. The surgeon's first impression was that it represented endometrial implantation, but on further exploration he found that it consisted of a discrete cyst of the left ovary with a twisted pedicle. It was possible to free it and to remove it without difficulty. When the cyst was opened it was found to contain cheesy material and hair, in other words, it was a dermoid cyst of the ovary, with a twisted pedicle.

DR. MILLER: Had it ruptured?

DR. MALLORY: No.

CASE 32462

PRESENTATION OF CASE

First admission. A seventy-four-year-old woman, a lecturer, entered the hospital because of substernal pain.

For twenty years the patient had had an insidiously developing productive cough that was worse during the winter and when she caught cold. The amount of thick, white sputum gradually increased to an estimated two cupfuls daily at the time of entry. Four years before admission she raised blood-streaked sputum for three days. For several years she had stopped giving long lectures because they made her hoarse. Seven years before admission the patient became dyspneic and gained weight. X-ray examination showed a large heart. With digitalis the symptoms gradually cleared until five years before admission, when a dull ache developed throughout the chest. It was accompanied by exertional dyspnea, anorexia and a loss of 10 pounds in weight. Thereafter the ache was almost constant and was not affected by deep breathing but was made worse by exercise. During these five years there was little change except for increasing fatigability. The day before admission, after walking half a block, the patient felt as if the chest were being squeezed. She walked a little farther and had to call a taxi. The sensation was described as if "something were expanding in the chest" causing pressure and pain that were mostly substernal but radiated all through the chest. She was dyspneic and weak and had difficulty in talking.

The patient had married at the age of nineteen and had one child, who was in good health.

On examination the patient was in no apparent distress except for a cough productive of sticky white sputum every three or four minutes. There were bilateral cataracts obscuring the fundus, although the patient could read. The left heart border extended 10 cm from the midsternal line in the sixth interspace. The sounds were good. Inconstant, coarse rhonchi, which disappeared on coughing, were heard throughout the chest. The diaphragm was low, and the excursions were poor.

The temperature was 99°F, the pulse 90, and the respirations 20. The blood pressure was 150 systolic, 90 diastolic, in the left arm, and 130 systolic, 100 diastolic, in the right arm.

Examination of the blood showed a hemoglobin of 12.6 gm per 100 cc and a white-cell count of 9400. The urine gave a ++ reaction for albumin, and the sediment contained 35 white cells per high-power field. An x-ray film showed marked dilatation of the ascending arch and proximal descending portions of the aorta. The true diameter appeared to measure about 6 cm. The aorta was tortuous and contained calcifications. The trachea was compressed and displaced toward the right. The pulsations of the aorta were not wide. The left

a final cause of death to explain the dyspnea. With paroxysmal attacks one might also consider the possibility of pulmonary embolism, but certainly only as a final complicating episode.

First of all, I should say that this woman undoubtedly had an aortic aneurysm. In spite of her age and the negative serologic findings, it was probably syphilitic. I am almost forced to discard a dissecting aneurysm, in spite of the x-ray picture, because I believe that on the evidence presented it is less likely than syphilitic aneurysm. I think it quite likely that the terminal event was the result of myocardial infarction and congestive heart failure.

DR. TRACY B. MALLORY. Does anyone wish to support the possibility of dissecting aneurysm?

DR. BLAND. I should like to add that this patient presented a problem from the psychologic point of view. Quite properly, the question was raised why she went home so soon. Her physicians did not have much choice in the matter.

CLINICAL DIAGNOSES

Aortic aneurysm, arteriosclerotic type
Coronary occlusion

DR. WILLIAMS'S DIAGNOSES

Syphilitic aortitis, with saccular aneurysm of thoracic aorta and rupture.
Myocardial infarction and congestive heart failure?

ANATOMICAL DIAGNOSES

Syphilitic aortitis, with multiple fusiform and saccular aneurysms of thoracic aorta
Rupture of aorta, with pseudodissection
Media necrosis cystica of aorta
Compression, left main bronchus
Bronchiectasis, left lower lobe
Atelectasis, left lower lobe

PATHOLOGICAL DISCUSSION

DR. MALLORY. The significant pathologic lesion was in the aorta. There was a large fusiform aneurysm involving the entire thoracic aorta and, in addition, localized saccular outpocketings, one of which was just beyond the innominate vein and definitely pressed on and narrowed the bronchus to

the left lower lobe. The bronchial tree in this lobe was diffusely dilated. The bronchi were plugged with partially inspissated mucous secretions, and the lobe itself was diffusely atelectatic. The gross appearance of the aorta was characteristic of syphilis, although the process did not extend quite down to the aortic annulus. There were also two rents in the intima of the thoracic aorta, not associated with either of the saccular aneurysms. One of these was quite small and contained a small partially organized blood clot. Beneath the larger rent there was an area of apparent dissection 5 or 6 cm. long filled with partially organized blood clot, some 2 cm. in thickness. On microscopic and gross examination it seemed apparent that this was not a true dissecting aneurysm, which always occurs within the media of the aorta, but a pseudodissection between the outer border of the media and the adventitia—a type of lesion that could occur with rupture of either a syphilitic or a sclerotic aneurysm. The microscopic sections were quite interesting. There were areas presenting all the accepted criteria of syphilitic aortitis, focal destruction of the elastica and muscularis and marked infiltration with lymphocytes and plasma cells in the areas of scarring and also in the form of cuffs around the vasa vasorum. In another part of the aorta there was also characteristic media necrosis cystica, which is the cause of the great majority of dissecting aneurysms. According to standard teaching, syphilitic aortitis and media necrosis cystica are not supposed to exist together in the same aorta. I think that there is no question that in this case they did. It is even conceivable that this was true dissection, although our decision was that it was not. After careful study we found nothing that clearly explained the acute terminal episode. There may have been a little more hemorrhage in the aortic wall, which we could not clearly separate from the previous bleeding. It is quite clear that the majority of the leakage must have occurred at the first attack rather than at the second.

DR. WILLIAMS. What about the heart?

DR. MALLORY. It was normal. There was not much evidence of chronic passive congestion. The lungs weighed 1100 gm. and were moderately edematous. The liver, spleen and kidneys did not show passive congestion.

is significant. Such a difference may result from aortic aneurysm, and it is sometimes seen in dissecting aneurysm of the aorta.

DR JAMES R. LINGLEY: There is marked dilatation of all the thoracic aortic shadow extending up over the arch and down in the descending portion. The heart shadow appears to be enlarged, and there is density at the left base. In this oblique view there appears to be pressure on the left main bronchus. Another thing that I should like to draw attention to is that the calcification in the arch of the aorta has a peculiar rim—instead of being in the periphery it lies 1.5 cm. within the shadow.

DR BLAND: Could that be due to the position of the patient?

DR LINGLEY: I do not believe so.

DR WILLIAMS: Is the left bronchus elevated?

DR LINGLEY: It seems to be compressed.

DR WILLIAMS: The early symptoms described before admission certainly suggest, more than anything else, expanding aneurysm of the aorta. There is really nothing inconsistent with that diagnosis except perhaps the long period of survival following the onset of early symptoms, which is unusual for a syphilitic thoracic aneurysm. If the patient had had thoracic aneurysm on a syphilitic basis it would be reasonable to assume that the chest pain resulted from sudden expansion of such an aneurysm. The earlier symptoms of blood spitting, pain in the chest and so forth are classic.

Dissecting aneurysm, of course, should not be overlooked. Cases have been reported in which the patient survived the initial dissection for many years. I am not quite clear about Dr Lingley's statement of the inner lining of the shadow with calcium, unless it means that the original coat of the aorta was covered over with blood clot. I suppose that that could happen in a leaking saccular aneurysm of the aorta or dissecting aneurysm as well, in the former, blood might infiltrate the outer adventitia. In considering the possibility of dissecting aneurysm, one might quibble over the time of survival following the symptoms that led to admission. Several days elapsed, but it is not too incompatible with dissecting aneurysm for the patient to survive several days before death finally supervenes. From the evidence, I favor a slowly expanding thoracic aneurysm rather than a sudden dissection. It is also possible to have a dissecting aneurysm complicating syphilitic aortitis. Such cases have been reported, in spite of the fact that syphilitic aortitis is supposed to have an annealing action, theoretically effective in preventing dissection. Against the diagnosis of syphilitic aortitis in this case is the patient's sex. The ratios of male to female vary from 5:1 to 8:1, depending on the series recorded. Of course, that is not of importance as a deciding point, nor is the age against the diagnosis of syphilitic aneurysm. The negative blood

Hinton reaction is disturbing but is not final evidence against syphilitic infection. The original process could have burnt out or the test may have been negative because of the so-called "zone phenomenon." If the patient had syphilis it was more probably a burnt-out infection.

During the hospital stay the temperature rose to 100 and 101.5°F daily. Apparently, the house staff was not impressed with the possibility of coronary insufficiency or myocardial infarction to explain the more recent symptoms, because they allowed the patient to go home after a week in the hospital. Nevertheless, I think that this is a possibility, in spite of the apparently normal electrocardiogram. Sometimes, more than a week elapses between the onset of infarction and appearance of the classic changes in the electrocardiogram—as long as three weeks may elapse before a definite diagnosis is possible. I am unable to explain the fever except possibly as a result of myocardial infarction, which would also be consistent with the rapid sedimentation rate.

At the final admission eleven days later, the patient had a smothering sensation and difficulty in breathing followed by coughing, but nothing is said about the character of the cough. There was a slight drop in blood pressure. At this point something else had happened. She developed acute dyspnea and venous engorgement, and the liver was palpable. The best possibility to explain that is congestive heart failure. On that basis, the only explanation we have found so far is myocardial infarction. Another possibility is that this was not heart failure. With aortic aneurysm, especially one involving the arch, it is possible to have obstruction in the venous system supplying the neck and upper extremities by expansion of the aneurysm. If we consider that the acute pain before entry was produced by expanding aneurysm, which is possible, venous engorgement may also have been caused by the same thing. Slightly against that supposition is the fact that no dilated veins were described over the rest of the chest. As a rule, with such complete obstruction, the whole upper venous system becomes distended. If the liver had been enlarged because of venous obstruction, however, that would mean obstruction of the lower systemic venous circuit as well. Such widespread increase in venous pressure is oftener the result of congestive heart failure than of mechanical obstruction.

One other question I should like to bring up regarding the aneurysm is whether this could all have been caused by arteriosclerosis. Arteriosclerotic aneurysm of significant size is more frequently seen along the course of the abdominal aorta than in the chest, although I believe that such aneurysms have been found in the chest. I do not recall ever seeing one that produced a significant mechanical effect by expansion, but I suppose that that is another possibility that must not be overlooked as

one of the most valuable agencies that the people of Massachusetts possess

It is common knowledge that modern, universally accepted public-health methods include keeping schools open during epidemics, except under certain specific circumstances, enlightened health and school officials believe that the safety of children is better guarded by having them under daily surveillance rather than running at large. Furthermore, common sense leads to the conclusion that the public is better served by having its confidence in its deserving public-health servants strengthened, rather than disturbed, by indiscriminate alarms and uninformed criticism. Massachusetts is fortunate in possessing a department of public health with an able, honest and experienced personnel, and Newton has an outstandingly capable health officer. Any attempt at discrediting either of them must be considered as subversive of the public welfare.

The physicians of the Commonwealth should accept the responsibility of maintaining public confidence in these agencies and will no doubt be aided in the task by so honest a journalist as Mr. Cunningham when he realizes the harm that his temporary aberration may have caused.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

DWYER—William J. Dwyer, M.D., of Boston, died September 30. He was in his sixty-fourth year. Dr. Dwyer received his degree from Tufts College Medical School in 1905. He was a fellow of the American Medical Association. His widow, a son and a daughter survive.

HOLBROOK—Bradbury Holbrook, M.D., of Waltham, died August 24. He was in his seventy-fifth year. Dr. Holbrook received his degree from University of Pennsylvania School of Medicine in 1899. He was a fellow of the American Medical Association.

HOLT—William L. Holt, M.D., of Amherst, died October 18. He was in his sixty-eighth year. Dr. Holt received his degree from Harvard Medical School in 1905. His widow, two sons and two daughters survive.

PULSIFER—Walter H. Pulsifer, M.D., of Whitman, died September 26. He was in his sixty-third year. Dr. Pulsifer received his degree from Tufts College Medical School in 1908. He was president of the Plymouth District Medical Society and a fellow of the American Medical Association. His widow and three sons survive.

TERRY—Theodore L. Terry, M.D., of Stow, died September 28. He was in his forty-eighth year.

Dr. Terry received his degree from University of Texas School of Medicine in 1922. He was assistant professor of ophthalmology at Harvard Medical School and was a member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, Association for Research in Ophthalmology and New England Ophthalmological Society, and a fellow of the American Medical Association.

His widow survives.

MISCELLANY

HARVARD SCHOOL OF PUBLIC HEALTH

Expansion of Harvard University's School of Public Health through two important faculty appointments and the institution of two new degrees in research were recently announced by Brigadier General James S. Simmons, dean of the school. Those joining the staff are Dr. Hugh R. Leavell, formerly assistant director of the Division of Medical Sciences, Rockefeller Foundation, and Dr. John C. Snyder, former member of the United States Typhus Commission. In addition to degrees that presuppose the qualification of Doctor of Medicine, the school has added the degrees of Master of Science in Hygiene and Doctor of Science in Hygiene, which are open to research workers. Thus the investigation of problems connected with public health, as well as instruction, will be augmented. Dr. Leavell will occupy the chair of public-health practice, which became vacant in July owing to the death of Dr. Edward G. Huber. Dr. Snyder has been appointed professor of public-health bacteriology, a new chair created by the reorganization of the school.

When the United States Typhus Commission was organized during the Second World War, Dr. Snyder was appointed as a member. As such he studied typhus fever at close range in the Middle East and Italy. Since his release from the Army in 1945 he has been in charge of a program of typhus investigation sponsored by the International Health Division.

YALE INSTITUTE OF OCCUPATIONAL MEDICINE AND HYGIENE

Dr. Francis G. Blake, dean of the Yale University School of Medicine, recently announced the establishment of the Institute of Occupational Medicine and Hygiene for work in the field of industrial medicine. The institute, Dr. Blake revealed, will be headed by Dr. Ronald F. Buchan, newly appointed assistant professor of industrial medicine. The primary aims of the institute, according to Dr. Blake, are four in number: the training of medical students and industrial physicians, based on the belief that occupational medicine and hygiene now comprise a specialty, special graduate instruction, together with the opportunity for research in the field of occupational medicine and hygiene, which will be available to graduate students in medicine, nursing, public health and engineering, research in occupational medicine and hygiene, in the belief that the maintenance of active research in such an important field is of teaching value to the intelligent student, and consultation, whereby the institute will assist industrial concerns on certain practical questions in the same fashion as the clinicians in the School of Medicine assist their colleagues with regard to medical, surgical or public-health problems. The establishment of the Institute was preceded by nearly six years of planning and investigation, conducted on the premise that Connecticut, although relatively small in area, is one of the great industrial states and therefore has real need for work in the field of industrial medicine.

The program will be supervised by a special committee composed of the following members of the Yale Faculty: Dean Blake, serving *ex officio*, Dr. William T. Salter, professor of pharmacology, Dr. George M. Smith, research associate in anatomy, Dr. Ira V. Hiscock, professor of public health, and Dr. John R. Paul, professor of preventive medicine. This committee will serve as the co-ordinating group that will work with Dr. Buchan, the clinical director, in plan-

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GREATER BOSTON COMMUNITY FUND

THE drive to raise the \$7,000,000 necessary to support the 1947 needs of the three hundred and thirty Red Feather hospitals and health, youth and social agencies is now in full swing. The question that lies squarely before the people of Greater Boston, according to Mr. John E. Lawrence, chairman of the campaign, is as follows: "Are we going to enable the Red Feather Services of the Greater Boston Community Fund to carry on those humane activities that have made this community renowned for its social consciousness?" The alternative, as Mr. Lawrence points out, is a sharp curtailment of essential services or their maintenance on a bare minimum-need basis—either of which is unthinkable.

The total that must be raised is nearly as large as those of the war years, in spite of the fact that support of certain agencies engendered by the war has been withdrawn. This, however, is not surprising when it is realized that the costs of food, wages and deferred maintenance have increased by at least 40 per cent. "The challenge is put to every one of us," declares Mr. Lawrence. "I firmly believe that the decision will be to keep the community strong. It is up to all of us to force that decision, and I call on every worker and every giver to do just that. We must RING THE BELL!"

A REGRETTABLE INCIDENT

It is unfortunate that "Bill" Cunningham, justly celebrated columnist of the *Boston Herald*, should have abandoned all restraint in his column of October 27 that commented on the recent postseason outbreak of poliomyelitis in Newton. At the time of the appearance of this article, 12 cases of infantile paralysis had appeared in that city since October 1, of which 9 had occurred in a certain school district. The school in question had not been closed on account of the outbreak, and this apparently seemed to Mr. Cunningham to have been a dereliction in duty on the part of city and state health authorities and aroused his sense of personal responsibility to the public. Possibly he was somewhat "hyper-sensitive" to the matter because of certain broad comments he had only recently made concerning pollution of the Merrimac River with poliomyelitis virus, a statement in support of which evidence is still lacking.

Regrettably, Mr. Cunningham in his investigation appears not to have used the probe but rather the bludgeon, and to have become inflamed at, rather than appreciative of, the methods of the highly trained officials who constitute the health departments of both the Commonwealth of Massachusetts and the City of Newton. It is with little real insight into the problems and the difficulties of public-health administration that Mr. Cunningham allowed such a statement as "Health Guardians Need Lesson in Humility to Public, Parents" to appear over his signature, it is unworthy of this protagonist of the common good to attempt to discredit

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MEDICINE IN THE POSTWAR WORLD*

MORRIS FISHBEIN, M.D.†

CHICAGO

IT IS well known that medicine in the postwar world will be far different from what it was at the end of World War II. The many advances, the great economic changes in the condition of peoples all over the world and the difference in the planning and organization of civilization make it folly to believe that in the years to come the status quo can be maintained or the life of previous generations enjoyed. A list of the discoveries that came out of the war through the co-ordinated and integrated research that was carried on reveals at once the great changes that have occurred in the practice of medicine. Unfortunately, medicine knows far more about the changes than the people, who benefit by the progress.

In World War I, 24 per cent of the soldiers who developed pneumonia died, whereas in World War II, less than 0.5 per cent died. That is, of course, a tremendous fact and an indication of the discovery and application of the sulfonamides, the antibiotics and penicillin, as well as a representation of the extent to which a significant discovery alters the entire picture of medical practice more than any amount of organization, administration or legislation.

An example is afforded by the change in the control of venereal disease, particularly as a result of new methods of treatment employing the antibiotic drugs. For more than a hundred years, in efforts to stamp out venereal disease, millions of dollars of federal money have been expended in the United States, without conspicuous success. Yet it is safe to predict that an application of the newer knowledge of control that has resulted from the war—the treatment of gonorrhea by the sulfonamide drugs and the intensive therapy of syphilis by the use of penicillin and heat and the newer arsenicals—will, within a quarter of a century, render these two venereal diseases as rare as typhoid fever and diphtheria are today. The progress in the control of typhoid fever and diph-

theria in the last fifty years was accomplished not by the spending of vast sums of money, by the invoking of the police or military powers of the nation or by the passing of new legislation but by invention and discovery in the field of medicine and particularly by the high state of knowledge developed by the medical profession.

Americans are proud of the fact that in the United States medical education leads the world. In no other country do medical schools approach the standards achieved by American institutions, nor is medical research in other countries comparable. There are no hospitals capable of rendering a higher quality of medical service than that furnished by the hospitals of the United States. It is therefore probable that physicians all over the world, for the next generation, if not for the next hundred years, will look to and will visit the United States in search of the benefits achieved by the advance of medical knowledge.

In World War I slightly over 9 per cent of men with wounds of all types died, in World War II less than 3 per cent died of their wounds. In World War I, chest wounds were fatal in 70 per cent, in World War II, in the Army of the United States, 20 per cent—but in the German Army 70 per cent—of men wounded in the chest died of their wounds.

These well established statistics bear testimony not only to the great discoveries in the treatment of injuries and disease but also, of course, to the quality of medical knowledge and medical practice in the United States. It is true that the application of blood transfusions and blood plasma and the various derivatives of blood, many of which had already brought about great changes in the control of diseases of various types, played a vital part in the saving of lives from shock and hemorrhages. It is also true that the antibiotic drugs eliminated the secondary infection associated with wounds of the chest and abdomen, but Dr. Kirk, Dr. McIntire or any of the great medical leaders of the armed forces of the United States would give the credit not only to these drugs but also to the high quality of surgical work and to the fact that such

*Presented at the annual meeting of the New Hampshire Medical Society, Manchester, May 14, 1946.
†Editor, *Journal of the American Medical Association*.

ning the work of the institute at the inauguration of the program. Dr Buchan, who will sit with the committee, has been practicing industrial medicine in Hartford, where he has been concerned primarily with the organization of medical services for a group of small industrial plants

BOOK REVIEWS

What People Are. A study of normal young men. By Clark W Heath, M.D. In collaboration with Lucien Brouha, Ph.D., Lewis W. Gregory, Carl C. Seltzer, Ph.D., Frederic L. Wells, Ph.D., and William L. Woods, Ph.D. A publication of the Department of Hygiene, Harvard University, under a grant from the Grant Foundation. 8°, cloth, 141 pp., with 7 tables. Cambridge: Harvard University Press, 1945. \$2.00.

This book is the result of the study of students at Harvard University, begun in 1938. The author, in collaboration with his colleagues, made a study of over two hundred and fifty young men from various points of view. It was not easy to pick out the "normal," for in the first hundred supposedly healthy men studied, seventy-two requested some sort of advice and another twenty-two presented urgent problems, mostly on the basis of a choice of a career, social adjustments or personality difficulties. An attempt was made to study the normal personality and the degree of adjustment to college life — as illustrated by athletic participation and their problems concerning religion, sex and other matters. Physiologic and mental measurements were made, and general medical problems were also investigated. This report discusses various aspects of these problems and is a valuable addition to knowledge in this field. It is only a preliminary study and should lead to more extensive research. The material presented, however, is of interest to physicians, particularly those associated with colleges, and to sociologists, educators and psychiatrists.

Lights Out. By Baynard Kendrick. 8°, cloth, 240 pp. New York: William Morrow and Company, 1945. \$2.50.

This is the story of a soldier in World War II from the time he was rendered totally blind by a sniper's bullet, until he was completely conditioned to take his place in the world of today. The psychology of the blind veteran is vividly portrayed, and interesting and accurate descriptions are given of the therapy and methods of rehabilitation practiced at the Valley Forge General Hospital, Pennsylvania, and the Old Farms Convalescent Hospital, Avon, Connecticut. This novel is an important contribution to the medical history of World War II.

Government in Public Health. By Harry S. Mustard, M.D., LL.D. 8°, cloth, 219 pp., with 11 tables. New York: The Commonwealth Fund, 1945. \$1.50.

This monograph was prepared at the request of the Committee on Medicine and the Changing Order of the New York Academy of Medicine. The letter of invitation read: "What is wanted is not merely a survey of the present situation, but knowledge of how it came to be, perspectives to help chart the direction of future developments."

The scope of public health is outlined, federal health services, state health departments and local health departments are described, and future trends are discussed. The following quotations from the book describe its contents:

First, there has always been, and there is now more than ever, a trend toward a more powerful federal government and, second, there has recently developed a strong trend toward a more socialistic federal government. Pertinent in this connection is the fact that public health activities are more and more being considered as an integral part of the developing social security program and are receiving increasing federal attention.

This document is to recognize political and social evolution as it relates to the public health, to view these things as nearly objectively as possible, to regret the passing of earlier concepts and manners, and to confess to a belief that a better public health will result from the changing order.

To those who do not approve of some of the social and governmental trends of today, it is suggested that it is

more profitable to recognize their enemy's approach and dimensions than it is just to swear at him after being blinded by temper.

This volume should be read by members of the public health profession and will be a valuable addition to the library of practitioners of medicine.

NOTICES

ANNOUNCEMENTS

Dr. G. Burnham Beaman announces the removal of his office from Boston to 322 Main Street, Stamford, Connecticut, and the inauguration of a psychiatric service and outpatient clinic in psychiatry at the Stamford Hospital.

Dr. Paul J. Catinella announces the opening of his office for the practice of dermatology and syphilology at 520 Commonwealth Avenue, Boston.

Dr. Samuel H. Marder, having returned from military service, announces the opening of his office for the practice of psychiatry at 419 Commonwealth Avenue, Boston.

Dr. Bernard Yood, recently discharged from military service, announces the opening of his office at 481 Beacon Street, Boston, for the practice of psychiatry and neurology.

EDWARD K. DUNHAM LECTURES

The Faculty of Medicine of Harvard University has announced that the following lectures on the general topic "Biochemical Lesions and British Anti-Lewisite" will be delivered by Dr. Rudolph A. Peters, Whitley Professor of Biochemistry, Oxford University, under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences.

Monday, November 18 The Significance of Biochemical Lesions

Wednesday, November 20 The Arsenical Lesion and its Antidote

Friday, November 22 Clinical Applications and Developments of BAL

These lectures are scheduled for 5 p.m. at the Harvard Medical School, Building C Amphitheater.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

A meeting of the New England Society of Physical Medicine will be held at the Veterans Hospital, West Roxbury, on Wednesday, November 20, at 8:30 p.m.

PROGRAM

Clinic on Physical Medicine with Case Presentations

Dr. Jacob Rudd

Medical Rehabilitation in the Veterans Administration

Dr. Sidney G. Licht

Discussion: Dr. Arthur L. Watkins

CANCER TRAINEESHIPS

Dr. Thomas Parran, surgeon general of the United States Public Health Service, Federal Security Agency, has recently announced that the National Cancer Institute, which operates as a division of the National Institute of Health, has funds to train approximately thirty physicians in the diagnosis and treatment of cancer. Under a federally financed program, doctors wishing to specialize in this field may be appointed as trainees and be assigned to authorized nonfederal, nonprofit institutions in various parts of the country. Applications for traineeships should be sent to the Director, National Institute of Health, Bethesda, Maryland.

(Notices continued on page xxi)

the specific request of President Roosevelt, to rehabilitate 2000 men, rejected because of such conditions as hernia and flat feet, sufficiently to render them capable of physical service in the Army. I assure you that the total number of men made available by that particular technic did not justify the extension of the project on a nationwide scale. Such figures and facts have never yet been presented at the hearings before the Senate Committee on Education and Labor.

In the period before the war, the Nation was well hospitalized, and it was accepted that 5 beds per 1000 people were adequate for any community. As a result of the advances in medical science, the new technics in surgery brought about by cyclopropane and basal anesthetics and the application of the antibiotic drugs, there is no longer the need for the number of hospital beds once demanded for a community of any size. It is now estimated that 35 beds per 1000 people instead of 5 provide adequate hospital facilities for a community. That is because, from 1912 to 1919, a patient entering a hospital for an operation for appendicitis could reasonably expect to spend fifteen to nineteen days in the hospital, whereas today the average stay is nine days, in many institutions, women who were formerly confined to bed for fourteen days after childbirth are now permitted up on the second or third day and plan to leave the hospital on the tenth day. Most of this change has been effected by the use of physiotherapeutic methods, amino acids and the vitamins, preoperatively and postoperatively, which also represent the advance of scientific medicine and the application of scientific methods under the best possible conditions, as well as the high state of medical education in the United States.

In considering postwar medicine, one must envision a still wider extension of the facilities of high-grade medical education to more and more people of the country. At the present time there are seventy Class A medical colleges and five new Class A medical colleges that are either opened or in process of being opened. With these new developments, I am quite sure that the schools in the New England states will be still further extended, and that high-grade medical education will be open to more and more young men who want to fit themselves for a career of service to mankind, with a reasonable amount of prestige and dignity, again provided that the legislators are not so shortsighted as to make it undesirable for a young man to seek a career in one of the greatest professions the world has ever known.

As I look over at what is happening in Great Britain, I shudder for the future of medicine there. The nation proposes to take over — in the old sense in which Al Capone used to "take over" — the medical profession and the hospitals, which will be administered as state institutions. So far as the

physicians of Great Britain are concerned, when the Minister of Health was asked what the income would be in the future, he replied, "A physician may reasonably expect to earn an income of \$5200, and after twenty years he may reach \$7200." That is the future offered to the physicians of Great Britain when the new health act proposed by the Ministry of Health becomes effective — if it ever does become effective. Because I am certain, knowing the people of Great Britain as I believe I know them, that, after five or ten years of what will happen to medicine under such a scheme, there will probably be a reversal of sentiment as great as that in other countries that have destroyed their own medical professions.

At this point, I wish to pay tribute to the industries associated with medicine in the United States. In a recent publication written by John Langdon Davis, of the British Bureau of Information, great tribute was paid to the pharmaceutical industry of the United States, which bears much of the prestige and honor for the winning of the war, because of its magnificent job of mass production that resulted in the saving of the health and lives of the soldiers and sailors of Great Britain, Russia and China, as well as of Americans. This achievement was made possible by the mass production of penicillin in this country in which twenty-three industries produced the drug at a rate that would have been inconceivable had not this great genius for mass production been applied. I remember sitting in on the first conference on penicillin with Dr. Florey at the National Research Council in Washington, where American manufacturers predicted that in three years 400 million units of penicillin a month might be produced. Last month, more than a billion and a half units of penicillin was produced. That means that the United States today is serving all the world with that antibiotic drug. No other country, including Great Britain, which has most of the honors for the discovery of penicillin, has even approached that level of mass production. Brazil and France are still trying to produce it in amounts of two quarts, we are producing it in ten-ton tanks. That is the difference between the genius of mass production of the United States and that of other countries. More factories are now being built, at a cost of millions of dollars, for the production of streptomycin, and such American advances as blood and blood derivatives, streptomycin, penicillin, DDT, Atabrine and 6718 for malaria mean that for at least a generation no other country can hope to approximate, much less equal, the progress of the United States in the advance not only of medical science but also of the industries associated with medicine.

This progress means little to the American people, unless its fruits can be made freely and generally available to all who require them. No one wants more than the doctors of the United States and the

excellent medical and surgical care was available even in the front lines

That is a testimony to the 60,000 American physicians who left their practices and the work they had built up for many years and entered the service. In 1940 there were over 180,000 physicians in the United States, of whom 150,000 were licensed to practice, and of those actually in practice 60,000 went out from their homes, offices and hospitals into the service of the Army and Navy. Today, something like 32,600 doctors have already been discharged from the Army and 6700 from the Navy. That means that about 40,000 of the 60,000 are now returning to their homes and communities to take up the work they left four years ago. It should be remembered that these men are returning to homes that have been broken up, to offices that have been taken up for other purposes and to communities in which the motor car and the facilities of medical practice have to some extent been eliminated. It must therefore be recognized that, overnight or in a year or two, the kind of medical practice that was generally available in the prewar years cannot be restored. Before the war there was 1 doctor to every 700 people, today, there are at least three counties in the United States in which there is only 1 doctor to more than 10,000 people. It is obvious, of course, that under those circumstances the medical care of the nation will suffer from a considerable number of inadequacies. It is unfortunate that the politicians and particularly the demagogues, who are endeavoring to lead the American people into strange ways of life far remote from the traditions of American democracy, should take advantage of unsettled conditions, which are clearly the result of war, and of inadequacies that everyone freely admits to bring about fundamental and complete medical changes in the United States. In promoting the proposed changes, they take advantage of strange statistics of one kind or another that are the height of folly and humor and would be so considered if the ultimate implications were not so serious.

Dr. Bauer has referred to the statistics of Selective Service, and I suppose that in all the hearings that have been going on in the last six weeks before the Senate Committee on Education and Labor (and I hope that some of you have been reading the condensations of the hearings) the proponents of these fundamental and revolutionary changes have repeatedly called attention to the amazing and shocking statistics that, they believe, should startle the Nation into a complete revolution in medical care. They have no real interest in the kind of scientific evidence that the medical profession demands as a basis for any new change or complete revolution in medical practice. To prove their statements of "amazing" and "shocking," they cite such round numbers as the 40 per cent of men in the United States who were rejected as physically

unfit. They say nothing whatever about the obvious fact that, in the first attempt to obtain an army for Selective Service before entry into the war, the highest standards of physical fitness developed for any army in the world at any time were employed. It will be remembered that at first the requirement for teeth was six good teeth in the upper jaw and six in the lower jaw and that it was later determined that the teeth had to be opposite each other. On that basis, 20 per cent of the men examined were rejected before the standard had reached the stage of merely counting the number of teeth in the jaws. Of course, it is quite impossible, if an Adonis is set up as the standard of physical fitness in men, to select a considerable number of people, or to pick out a considerable number of women if a Venus is the criterion. I believe that I should even have a little difficulty in this audience to reach that standard of physical perfection. Yet that was what was attempted in the Army when Selective Service was first in effect.

It is the humor of a nation that really reflects the nation's point of view. Before V-J Day, it was frequently stated throughout the country that if a boy who came up for the draft was still warm, he was in. And that represented, of course, the changing standards of physical fitness that ultimately came about. And it should be borne in mind that the statistics that are being cited before the Congressional hearings are actually the analyzed statistics of the first 2 million men — out of a total of 19 million examined — who came up for examination in 1940 and in the early portion of 1941. The statistics of the war years offer an entirely different picture.

During the first portion of the war, 4 million men, of the total of 19 million examined, were rejected, including 800,000 illiterates — 800,000 men who never reached the fifth grade, in a nation in which public education is free, and in which public education in many areas is compulsory, as compulsory and as free as health care would be under the changes proposed. At the end of the war, I visited the Great Lakes Naval Training Station to see 600 men, formerly classified as illiterate but subsequently taken into the United States Navy, who lifted up a certain amount of garbage into a shovel and deposited it in a wagon, they performed the task efficiently, whether or not they were illiterate. And so, everything depends on one's standards. We should make clear to our senators and representatives that it is the standard by which one measures that determines one's condition.

Again, I should like to point out that early in the war, when I was at one time adviser to the Selective Service and associated with many of the committees set up by General Hershey, a pilot experiment was conducted covering the states of Maryland and Virginia, in which it was endeavored, at

and the CIO, but it got space. Most of the members of this audience know in a general sense about the National Health Program. But, if I were to ask what were the five points, since this is not "Information Please" evening, there might be some difficulty in making a reply. Perhaps I can get Clifton Fadiman to ask his experts some night to name the five points of President Truman's health program, the experts would probably know that it had something to do with compulsory sickness insurance, and they would not know the other points. There are four additional points to the program, however, and it is highly significant that the medical profession of the United States has given its wholehearted approval to them.

The medical profession favors the widest possible extension of medical facilities in the form of hospitals, diagnostic centers and health centers, so that a high quality of medical care can be available, wherever there are enough people to require a hospital or a diagnostic or health-center service. There are, of course, certain areas in the United States that could not possibly build or maintain for themselves even small institutions of the type proposed. It is well within the province of the Government to make the funds obtained from taxation available for the extension of such a program. The American Medical Association has approved Senate Bill No. 191 (the Hill-Burton Bill), which was passed by the Senate and is now in hearing before the House and is likely to become law. That bill will make available 5 million dollars a year for administration and 75 million dollars a year for adequate buildings and diagnostic centers. All a state has to do is to have the governor determine the number of hospital and health centers available and needed and make the required survey. The governor then applies to the proper board, which will have charge of the funds under the Hill-Burton Bill, to obtain the state's share of the appropriation. The bill is bound to result in a greater number of health centers than heretofore. Fourteen states, in anticipation of that legislation, have already appointed committees or boards to undertake the surveys, and as soon as the act is passed, their applications will be submitted.

In Oklahoma, the entire area of the state has been mapped out, with a dot on the map for every health center, district hospital and diagnostic institution required. The project will be developed about a great medical center in Oklahoma City, with a large hospital in association with the medical school that will be highly specialized in the fields of neuropsychiatry and infectious diseases, and there will be a children's hospital and a maternity hospital, all part of the educational center. The most remote areas of the state will be able, under the freedom and initiative of the medical

profession working with the government of the state, to set up a medical system in association with a voluntary hospitalization and sickness insurance system that will effectively blanket the state. Oklahoma is in the nature of a frontier state, but I am quite sure that many of the older states could do an equally good job, and I believe that more than fourteen states have already set up committees in anticipation of this type of service, of which, of course, organized medicine approves. That is the American way — the acme of the use of the voluntary service and the private initiative of the people to achieve desirable results.

Half the states do not have a public-health and preventive medical service, perhaps all of them do not need it. Dr. Bauer has pointed out that in some communities there are extremely few people, so that to maintain a health officer would be utterly foolish — all he would have to do would be to keep a census of the people he started with. In such a situation, of course, a medical center is unnecessary. A preventive medical district center within certain states will be required, however, to provide a proper preventive medical service covering a total number of people, rather than an area. Suitable technics will have to be worked out. Federal funds, under the extension of the existing Social Security Act, may be required to meet the need. Again, under the Emergency Maternal and Infant Care Bill, there could be under certain circumstances a considerable number of mothers who did not receive post-partum care in childbirth — I do not know the exact number. At the present time in the United States, 80 per cent of white women have children delivered in hospitals, the number among Negroes is considerably less. Sooner or later, a technic must be worked out providing for adequate prenatal care, delivery and post-partum care that will repay the nation in healthy mothers and children.

Maternal death rates have dropped in the United States almost unbelievably. Fifteen years ago, in Wisconsin, there were 400 maternal deaths a year, today, although there is a 15 per cent increase in population, there are only 100 maternal deaths a year. Such figures show what can be and has largely been accomplished by improvement in obstetric service, not under state control but through the advances in obstetrics, with the new knowledge regarding the use of narcotics and their effect on the avoidance of toxemia and eclampsia — all of which has resulted from the voluntary service of physicians, working in hospitals and carefully and scientifically recording the results.

But try to explain that to Senator Pepper. He has no background in the field of obstetrics — of that, I am reasonably certain. Nevertheless, he comes forth with a bill providing that every woman in the United States shall be entitled to complete obstetric care when she asks for it and, in addition,

associated professions to see the widest possible distribution of medical care. If it is necessary to create more organization in medicine, at the same time retaining the features of medical science that comprise its greatness, the medical profession, which has led in the organization of medicine in the United States above all other nations in the world, should be given a reasonable opportunity to develop the kind of organization that can deliver a high grade of medical practice under the conditions of a democracy.

I have bragged somewhat about medical organization in the United States. In what other nation in the world is there a profession that contains a membership like that of the American Medical Association, in which 127,000 out of 155,000 practicing physicians are represented? What other organization has produced anything resembling the publications of the American Medical Association? What organization anywhere in the world has produced the kind of services rendered by the bureaus and councils that standardize medicine on an exceedingly high scale? Drugs and chemicals have been standardized through the councils, which, by defining quality and wholly by the power of public opinion, have raised the standards of pharmaceutical products in the United States above those prevailing anywhere else in the world.

In the United States there are a considerable number of the sulfonamides, such as sulfapyridine, sulfathiazole and sulfaguanidine, there is one name for each type, and it is recognized that the drug will be known by that name. In England there are forty-seven different names for sulfanilamide, each one of which is presumably known to each doctor, so that he can choose the particular one that he wants to work with, there is nothing resembling the standardization of pharmaceuticals that obtains in this country. Through the Council on Foods and Nutrition, the American Medical Association has standardized the use of food products and has maintained rationality in the gradual development of the use of vitamins. The use of physical apparatus has been standardized, so that there is none of the quackery and charlatanism that prevail in many countries.

The Council of Medical Education and Hospitals has established criteria for medical colleges and hospitals. The American College of Surgeons protects the patient against the hospital and the surgeon, if need be, by the work of men in the field of pathology, who carefully collect these data, to provide a rational and scientific basis for surgery.

It is the desire of organized medicine to deliver a high quality of medical service, and the Council on Medical Service proposes to set up the standards for such service voluntarily ensuring the patient medical care of a high quality, which he has purchased. Unless such standardization under insured systems prevails, there will never be a

high quality of medical service. I am convinced by all the available evidence that if ever a nationwide system of compulsory sickness insurance, administered out of a single type of Social Security Board, should be inflicted on the people of the United States, an unprecedented deterioration in the quality and a breakdown in the ethics and delivery of medical service would ensue. The scandal and deterioration in the quality of medical service delivered to veterans in the United States under the previous Veterans Administration give an indication of what eventually occurs when medical service that ought to be personal, ethical and possessed of a high morale is subjected to the routine work and clock-watching activities that are invariably a part of that kind of medical service. One of the greatest services rendered to scientific medicine was the exposition of what happened to a centralized, bureaucratic control in the Veterans Administration, so that the people of the United States might know what to expect.

Medical practice in the United States in the postwar world offers the opportunity to apply medicine of a high type, developed in the highest quality of medical education and institutions and extended to all the people. Such an opportunity, to a scientist, entails some sort of diagnosis of the areas of need and the nature of the treatment to be applied when the area is determined. In the United States, of course, there are considerable inequalities in the nature and distribution of medical service. For instance, the two highest death rates for tuberculosis, if properly localized and focused in the areas of great need, are not among the Negroes in the South but among those in Newark and Chicago. Obviously, if the death rate from tuberculosis is to be lowered, attention must be focused largely, to begin with, on those particular spots.

It is known that when Wassermann and Kahn tests were conducted among the students of the University of Minnesota, 0.25 per cent showed syphilis. But similar tests on every inhabitant in certain Negro sections of the country showed a 33 per cent incidence of syphilis. Obviously, an attack on the problem of syphilis must begin in the area where it is 33 per cent prevalent, and not where there is an incidence of 0.25 per cent. If the area of need is determined and the remedy applied, a reasonable return on the investment can be expected. That, of course, is what is needed in the United States, to approach the problem from that point of view, the medical profession has already given all the aid it can to certain legislation that seems necessary for progress. Some time ago, Mr. Truman went before the Congress for the first time as President with what was called a "National Health Program." The program was mentioned in the press and on the radio—it did not receive as much attention as John L. Lewis

worker, who is promised health service over which he will have no control, this is called health insurance. I prefer to call it taxation to enable the Government to distribute political medicine throughout the United States. In the end, the plan is nothing more than the setting up of a vast political machine.

In some countries in the world having compulsory sickness insurance, there is 1 government employee for every 100 insured persons. This bill proposes to cover 120 million of the 135 million people of the United States, so that the figure, by careful accounting, might be 1,200,000 new government employees. I do not believe that so many will be involved, Mr. Murray and Mr. Pepper have repeatedly pointed out that a considerable social-security system has already been set up, including the Social Security Board, the district Social Security agencies and the local Social Security inspectors.

But what are the Social Security employees doing now? If they have enough to do, the whole sickness care of the United States cannot be added to the present Social Security system, which in its time has had, I might say, strange inadequacies. I said to Paul McNutt one day, "I understand that you have 8 million John Doe cards." He answered, "What's that? Wait a minute. I heard you, but I didn't know you knew." A "John Doe card" is a card in the files of a government bureau to indicate that contact has been lost between a man's number and what he has coming to him, his name has been separated from his number, or he and the card have been lost altogether. At one time there were 8 million John Doe cards. Paul McNutt told me that they had worked it down to a reasonable million cards. There are therefore a million cards of this type, because the American workers move around and bookkeepers get sick and the changes are not recorded.

I told the following story to Congressman Miller.

Here's a poor fellow with a gall bladder, he has a few stones, and one of them started off and it is not getting any place. So he is disturbed, he has pain, and he is suffering. He calls in a doctor and the doctor says, "This is a little heavy for me, I shall have to get you a specialist." The man doesn't want a specialist because he has confidence in the doctor, but the doctor tells him "This is outside of my range, I've got to get you a specialist. I'll get Dr. Smith for you." Well, the patient doesn't like Dr. Smith. "But you've got to take Dr. Smith because he is the one the Social Security Board says does that type of work." That makes no difference, he does not want him. Consequently, he files an appeal with the district Social Security administrator, who has no authority outside his own district and who does not want to overrule the decision, and is told "I am sorry, but Dr. Smith is the fellow that the Surgeon-General picked, and he is your man." But the patient still does not want Dr. Smith. In the meantime, he is vomiting and he has a little pain, and the gall bladder is getting quite annoying, if he is still alive. He therefore asks the Social Security Administrator, "What can I do?" Senator Pepper's answer to that question was that the patient could appeal to the courts over the decision of the Social Security Administration. The case, which is put on the docket, will come up in the session in October of the year following the date in which the gall bladder hurts — the patient finally gets to the courts.

The time may come when the Supreme Court of the United States will spend its time trying to find surgeons to remove John's gall bladder eight years after John has been cremated!

That gives an odd picture of what medicine could come to under that kind of administration. The President and Senator Wagner stated that the bill offers a free choice of doctors, which it cannot possibly do. In the first place, there are not that many doctors. A physician is not required to work under the system unless he wishes to do so, and most of them will probably not choose to do so for quite a considerable time. In addition, a doctor's number of patients is limited. It might well happen that one of you has been chosen by the good-looking women of this town, and along comes a not-so-good-looking-woman who wants to get on his panel, which is filled. She appeals to the Social Security administrator, who tells her that Dr. — must lose one of his present patients before he can take a new one. The woman replies, "I know the aldermen," or "I know the Governor, and he will see to it that I get on Dr. —'s list." So then, someone is removed from Dr. —'s list, and she gets in on the panel. Dr. — takes one look at her and says "I don't want her anyway!"

Such a story appears comical, I am telling it to be comical. But that is how the bill will work out. For Mr. Altmeyer granted freely to Senator Donnell of Missouri that if twelve doctors in Sedalia, Missouri, refused to work under the system, preferring private practice, the Surgeon-General of the United States, since the people in Sedalia had paid their insurance or their taxes, would send in physicians to take care of them. That is totalitarianism under the guise of compulsory sickness insurance, it is the equivalent of saying that if doctors do not want to work under the system, the Government will see to it that somebody is there to take care of the people who have paid their taxes or their insurance.

The Wagner-Murray-Dingell Bill, an unfortunate piece of legislation, in my opinion — based on a considerable amount of observation and evidence — will receive an interim report. When something pretty hot comes up in Congress, an interim report is issued. The following warning is given: "You fellows keep on working, or we may slip it over on you." That is the present position of this piece of legislation, and organized medicine must continue studying and working on it. Senator Murray stated not only to me but also to some of the witnesses present at the hearings "After all, we scared you fellows so much that you have really started to do something, whereas formerly you talked about it a great deal and didn't do very much." Being an honest man, I replied, "There's no doubt about that. You scared the boys considerably. The doctors are plenty disturbed, and they are moving faster than ever be-

that every child shall have complete medical care without cost up to the age of twenty-one years. Well, that baffled me. I have a boy nineteen years old, and he has been away from home for a long time, he is taller than I am, and I should hate to call him a child. Yet a senator of the United States proposes that the Government give complete medical care to all children up to the age of twenty-one years. I have estimated, and I think the figures are accurate, that there are 40,000,000 under twenty-one in the United States. For those children, granting each one of them \$10.00 a year for medical care, \$400,000,000 a year would be required. The addition of approximately 2,750,000 women each year giving birth to children and approximately 300,000 who could but do not result in an interesting figure. Consequently, the total of approximately 3,000,000 women, with a minimum of \$50.00 per woman for ordinary care, would involve as much money as is now spent in the United States for all medical care.

The problem of the aged today is the most serious of all the problems because there are so many of them among us. I remember that in the old days when the parents grew old the children helped care for them. Sometimes they took their parents into their homes, it was considered desirable to maintain the family as the center of life. In a democracy, the family must be preserved, or democracy will perish. But here is a proposal that the family be destroyed and that the state take care of the children and of the mothers in childbirth. One can imagine in the future long lines of children proceeding in a mass-production line up to some child specialist, associated with a social worker and a nurse, who perform inoculations and tell how the baby shall be fed (God knows where the mother is!). This is a picture of the breakdown of a democracy initiated through a scheme for the medical care of the mothers. But the medical profession considers the best medical care to be that of a mother by her own physician and that of a child by the family physician, with the mother present and not delegating her responsibilities to a state-controlled or a federal-controlled institution. It is quite possible under the existing social security act to provide that type of service.

During the war, under the Office of Scientific Research and Development and its committees and the National Research Council, the great scientific discoveries that I have mentioned were developed, and those advances should be extended. Senators Magnuson and Kilgore have introduced a bill with which the American Medical Association is in complete agreement, except on minor details concerning patents that are considered to have no place in the bill. Organized medicine is in favor of the continuation of the co-ordinated and intensified research that has so far yielded vast benefits. This bill does not propose to build federal research

institutions but to make sums of money available, beginning with \$125,000,000 the first year and \$250,000,000 in five years, 20 per cent of which is to be used under the direction of a medical board, the rest under the control of a basic science board, and the defense funds under the control of a defense board. This is all to be made available in existing institutions of education, existing hospitals and existing institutions of research, where young men can gradually develop from students into the kind of research men needed for that type of service. That is the third point of President Truman's health program.

The fourth point of the program provides that workers be insured, as they are now insured against loss of their jobs, and insured as they are now protected against old age, by an addition to their insurance, with protection against loss of wages due to illness. Obviously, that is the kind of protection that every worker needs. If a worker is out of work for fourteen or fifteen weeks because of illness and his employer has not worked out a plan for maintaining or continuing his income to support his family, that has to be the man's responsibility. If workers can be taught to save in time of employment against loss of wages due to illness, even under a compulsory plan, all they are doing is putting the money in a bank for use when they need it, they are still the owners and the bosses of the money, and no federal agent is distributing the money and telling them who shall take care of them. That is a sound application of the insurance principle.

But President Truman's fifth point, unfortunately, is one on which the medical profession not only does not see eye-to-eye with him but not at all. That is his compulsory sickness insurance which he took the trouble to say five times in his speeches was not socialized medicine. We have developed new jargons associated with economics, sociology and the social sciences that are difficult for a great many people to understand. I challenge you to understand what most psychoanalysts mean by the "id," "ego" and a few of the other things that are supposed to be disturbing the people. So that when those phases of the work are involved, strange jargons are used. But it makes no difference whether the plan is called "compulsory sickness insurance" or "compulsory health insurance," as its sponsors prefer to call it. It is health insurance in the propaganda sense, since the word "sickness" would be unfavorable to the propaganda. It is sickness insurance nevertheless.

The words "preventive medicine" occur only once in the one hundred and eighty-six pages of the bill. And, of course, the plan involves not insurance but taxation, because it is taxation of the worker and the employer—you pay the taxes, they collect and keep the taxes and they spend them. That is taxation. A tax is imposed on the

THE RECEPTION IN ENGLAND OF HENRY JACOB BIGELOW'S ORIGINAL PAPER ON SURGICAL ANESTHESIA

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IT IS not widely known that Henry Jacob Bigelow's original announcement concerning surgical anesthesia, which was issued in the *Boston Medical and Surgical Journal* on November 18, 1846, when its author was twenty-eight years of age, was reprinted at least four times within a few weeks of its appearance—twice with the omission of the final controversial paragraphs about the patent and twice in its entirety†.

The first reprinting, which included the entire text, appeared in the *Boston Daily Advertiser* on November 19, the day after it had been published in the *Boston Medical and Surgical Journal*. Eager to convey news of the great discovery to his friend Francis Boott, of London, Professor Jacob Bigelow, young Bigelow's eminent father, wrote a letter to him on November 28, in order to get it on the first boat sailing for Europe (December 1), and enclosed a copy of the *Advertiser* for the 19th. The text of this letter, which was published in the January 2, 1847, issue of the *Lancet*, has not often been reprinted and may therefore be of interest.

Boston, Nov. 28, 1846

My dear Boott, — I send you an account of a new anodyne process lately introduced here, which promises to be one of the important discoveries of the present age. It has rendered many patients insensible to pain during surgical operations, and other causes of suffering. Limbs and breasts have been amputated, arteries tied, tumours extirpated, and many hundreds of teeth extracted, without any consciousness of the least pain on the part of the patient.

The inventor is Dr. Morton, a dentist of this city, and the process consists of the inhalation of the vapour of ether to the point of intoxication. I send you the *Boston Daily Advertiser*, which contains an article written by my son Henry, and which is extracted from a medical journal, relating to the discovery.

Let me give you an example. I took my daughter Mary, last week, to Dr. Morton's rooms, to have a tooth extracted. She inhaled the ether about one minute, and fell asleep instantly in the chair. A molar tooth was then extracted, without the slightest movement of a muscle or fibre. In another minute she awoke, smiled, said the tooth was not out, had felt no pain, nor had the slightest knowledge of the extraction. It was an entire illusion.

The newspaper will give you the details up to its date, since which other operations have been performed with uniform success.

Several authors have stated that Henry Jacob Bigelow himself went abroad in December, 1846, to bear tidings of the ether discovery, but contemporary references to him in the *Boston Medical and Surgical Journal* indicate that he was definitely in

Boston during December, many also have erroneously attributed to him rather than to his father the letter addressed to Francis Boott.

On what day Jacob Bigelow's letter actually reached London is not known, but the crossing must have been, for those days, extraordinarily quick since the first reference in the British press to the use of ether appeared in the December 18 issue of the *London Medical Gazette*. This suggests that the vessel sailing on December 1 must have arrived in England at least by December 16, for two days gives small margin for delivering the letter, — which probably arrived at Liverpool, — abstracting its contents and setting it up in type. Since the text of this first announcement has not been alluded to in recent histories on anesthesia, it is given here.

ANIMAL MAGNETISM SUPERSEDED — DISCOVERY OF A NEW HYPNOPOIETIC

We learn on the authority of a highly respectable physician of Boston, U. S., that a Dr. Morton, a surgeon-dentist of that city, has discovered a process whereby in a few minutes the most profound sleep may be induced, during which teeth may be extracted, and severe operations performed, without the patient being sensible of pain, or having any knowledge of the proceedings of the operator. The process simply consists in causing the patient to inhale the vapour of ether for a short period, and the effect is to produce complete insensibility — or, as the writer says, intoxication. We quote the following case on the same respectable authority: "I took my daughter last week to Martin's [Morton's] rooms to have a tooth extracted. She inhaled the (vapour of) ether about one minute, and fell [fell] asleep instantly in the chair. A molar tooth was then extracted without the slightest movement of a muscle or fibre. In another minute she awoke, smiled, and said the tooth was not out, had felt no pain, nor the slightest knowledge of extraction. It was an entire illusion."

The facts are here so candidly stated that any one may put the new process to the test of experiment. Dr. Morton has made no mystery of his proceedings, like the tribe of hypnotic quacks who have lately perambulated the country. Some caution must, however, be observed in employing the vapour of ether in the way suggested. Ether is a strong narcotic, and its vapour speedily produces complete lethargy and coma, it is exceedingly volatile, and rapidly absorbed and diffused through the body, especially when brought into contact with the extensive surface of the air-cells of the lungs. In one case it has destroyed life, and in another caused apoplexy. Thus an individual may not awaken so readily as the young lady whose case we have here quoted. It must be regarded as producing a state of temporary poisoning in which the nervous system is most powerfully affected, and, as in concussion or narcotic poisoning, sensibility may be so destroyed that operations which in the healthy state would occasion severe pain, may be performed without any consciousness on the part of the patient. The respectability of the source from which we derive our information prevents us from doubting that the writer has accurately described what he saw. The awaking exactly *one minute* after the operation must of course be regarded as an accidental circumstance, depending on the dose of ethereal vapour inhaled. One statement, however, appears to us

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†A full description of the original communication and the four contemporary reprintings will be found in Fulton and Stanton's *The Centennial of Surgical Anesthesia. An annotated catalogue of books and pamphlets bearing on the early history of surgical anesthesia* (New York: Schuman, 1945).

fore" I also pointed out that, being doctors, they had not previously moved because they could not in honesty move—there were no statistics or actuarial data to warrant the selling of voluntary sickness insurance to the people of the United States with a guarantee that under any kind of sickness a high quality of service would be available.

In 1923 I held a conference all day with the Board of Directors of the Metropolitan Life Insurance Company and tried to persuade them to issue a cheap, voluntary sickness insurance policy on a cash-for-cash basis. But the Board of Directors and a vice-president stated that they could not do so and that they had no statistics on which to figure honestly the risk and the amount that should be paid, as well as no standards of physicians. Today, however, medical standards are on a higher level than those of 1923 and, if organized medicine has anything to say about it, will be kept at that level. Actuarial data are also being accumulated. The large insurance companies are now selling voluntary sickness insurance: the Metropolitan Life Insurance Company has fifteen hundred policies covering 1,700,000 people, and the Equitable Life Insurance Company has twenty-four hundred policies covering 2,800,000 workers in the United States. The policies of all companies represent 23 million workers in the United States who are now covered in whole or in part by various forms of sickness insurance. Few of them get complete coverage for any kind of illness, because the vast majority of American workers do not want such coverage—they want insurance against medical and surgical catastrophe and, sometimes, against obstetrics, which can be a catastrophe.

In addition, the Blue Cross is not what it was twenty-two years ago, it has begun to standardize on a definite level of hospital service and to make use of actuarial data—risks, even those of possible epidemics, are calculated. Twenty-four million people are now insured against hospitalization under the Blue Cross. Under the voluntary sickness plans of many states, the state medical society being the insurer or the controlling influence

and insuring commercially, five and a half million people are covered in the United States. The Council on Medical Service has standardized the plans under the Associated Medical Care Plans, Incorporated, so that a policy will be good from state to state, and will carry the seal of the American Medical Association as an indication that the policy is interchangeable and reaches the quality of service that the Association demands. That is progress.

Progress has also been made broadly through the Veterans Administration, and the medical care of veterans for service-connected disabilities has been extended to many of the states, within another year, most of the states will have organized their programs in such form that a veteran can apply to a doctor of his own choice and be treated in a hospital of his own choice that will meet the requirements of the medical society in the state concerned—all without centralized and federalized control.

Seventy-five million people in the United States carry 40 billion dollars' worth of protection in the form of life insurance that was sold to them by life-insurance agents on a voluntary basis. Yet the sponsors of compulsory sickness insurance tell me that voluntary insurance has never succeeded in any other country in the world—it has always moved into government insurance.

I say that democracy has never succeeded in any other country in the world as it has in our country. And I say, advisedly, that our country is the only country in the world in which democracy still has a chance, because we have the fundamental freedoms for which people fought many years ago: freedom of speech, thought, public assembly and worship, and the right of every man to make of himself the most that he can as an independent American citizen. If we guard those fundamental liberties, I am sure that we can continue to keep medicine in the postwar world on the same high level that it has reached.

535 North Dearborn Street

THE RECEPTION IN ENGLAND OF HENRY JACOB BIGELOW'S ORIGINAL PAPER ON SURGICAL ANESTHESIA

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IT IS not widely known that Henry Jacob Bigelow's original announcement concerning surgical anesthesia, which was issued in the *Boston Medical and Surgical Journal* on November 18, 1846, when its author was twenty-eight years of age, was reprinted at least four times within a few weeks of its appearance—twice with the omission of the final controversial paragraphs about the patent and twice in its entirety†

The first reprinting, which included the entire text, appeared in the *Boston Daily Advertiser* on November 19, the day after it had been published in the *Boston Medical and Surgical Journal*. Eager to convey news of the great discovery to his friend Francis Boott, of London, Professor Jacob Bigelow, young Bigelow's eminent father, wrote a letter to him on November 28, in order to get it on the first boat sailing for Europe (December 1), and enclosed a copy of the *Advertiser* for the 19th. The text of this letter, which was published in the January 2, 1847, issue of the *Lancet*, has not often been reprinted and may therefore be of interest

Boston, Nov. 28, 1846

My dear Boott, — I send you an account of a new anodyne process lately introduced here, which promises to be one of the important discoveries of the present age. It has rendered many patients insensible to pain during surgical operations, and other causes of suffering. Limbs and breasts have been amputated, arteries tied, tumours extirpated, and many hundreds of teeth extracted, without any consciousness of the least pain on the part of the patient.

The inventor is Dr. Morton, a dentist of this city, and the process consists of the inhalation of the vapour of ether to the point of intoxication. I send you the *Boston Daily Advertiser*, which contains an article written by my son Henry, and which is extracted from a medical journal, relating to the discovery.

Let me give you an example. I took my daughter Mary, last week, to Dr. Morton's rooms, to have a tooth extracted. She inhaled the ether about one minute, and fell asleep instantly in the chair. A molar tooth was then extracted, without the slightest movement of a muscle or fibre. In another minute she awoke, smiled, said the tooth was not out, had felt no pain, nor had the slightest knowledge of the extraction. It was an entire illusion.

The newspaper will give you the details up to its date, since which other operations have been performed with uniform success.

Several authors have stated that Henry Jacob Bigelow himself went abroad in December, 1846, to bear tidings of the ether discovery, but contemporary references to him in the *Boston Medical and Surgical Journal* indicate that he was definitely in

Boston during December, many also have erroneously attributed to him rather than to his father the letter addressed to Francis Boott.

On what day Jacob Bigelow's letter actually reached London is not known, but the crossing must have been, for those days, extraordinarily quick since the first reference in the British press to the use of ether appeared in the December 18 issue of the *London Medical Gazette*. This suggests that the vessel sailing on December 1 must have arrived in England at least by December 16, for two days gives small margin for delivering the letter,—which probably arrived at Liverpool,—abstracting its contents and setting it up in type. Since the text of this first announcement has not been alluded to in recent histories on anesthesia, it is given here.

ANIMAL MAGNETISM SUPERSEDED — DISCOVERY OF A NEW HYPNOSIS

We learn on the authority of a highly respectable physician of Boston, U. S., that a Dr. Morton, a surgeon-dentist of that city, has discovered a process whereby in a few minutes the most profound sleep may be induced, during which teeth may be extracted, and severe operations performed, without the patient being sensible of pain, or having any knowledge of the proceedings of the operator. The process simply consists in causing the patient to inhale the vapour of ether for a short period, and the effect is to produce complete insensibility—or, as the writer says, intoxication. We quote the following case on the same respectable authority: "I took my daughter last week to Martin's [Morton's] rooms to have a tooth extracted. She inhaled the (vapour of) ether about one minute, and fell [fell] asleep instantly in the chair. A molar tooth was then extracted without the slightest movement of a muscle or fibre. In another minute she awoke, smiled, and said the tooth was not out, had felt no pain, nor the slightest knowledge of extraction. It was an entire illusion."

The facts are here so candidly stated that any one may put the new process to the test of experiment. Dr. Morton has made no mystery of his proceedings, like the tribe of hypnotic quacks who have lately perambulated the country. Some caution must, however, be observed in employing the vapour of ether in the way suggested. Ether is a strong narcotic, and its vapour speedily produces complete lethargy and coma; it is exceedingly volatile, and rapidly absorbed and diffused through the body, especially when brought into contact with the extensive surface of the air-cells of the lungs. In one case it has destroyed life, and in another caused apoplexy. Thus an individual may not awaken so readily as the young lady whose case we have here quoted. It must be regarded as producing a state of temporary poisoning in which the nervous system is most powerfully affected, and, as in concussion or narcotic poisoning, sensibility may be so destroyed that operations which in the healthy state would occasion severe pain, may be performed without any consciousness on the part of the patient. The respectability of the source from which we derive our information prevents us from doubting that the writer has accurately described what he saw. The awaking exactly one minute after the operation must of course be regarded as an accidental circumstance, depending on the dose of ethereal vapour inhaled. One statement, however, appears to us

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†A full description of the original communication and the four contemporary reprintings will be found in Fulton and Stanton's *The Craniology of Surgical Anesthesia. An annotated catalogue of books and pamphlets bearing on the early history of surgical anesthesia* (New York: Schuman, 1946).

to require explanation. We can understand the production of insensibility and the temporary loss of consciousness from the effects of ether, but we do not comprehend how, when the individual was perfectly roused to consciousness, there could be the slightest doubt as to whether the tooth was in or out of the mouth! All who have undergone this operation know that from the imperfect sense of touch possessed by the tongue, that the gap occasioned by the loss of a tooth appears about ten times as large as it really is. Then, again, we can believe that no pain might be felt during the operation, but how can any narcotic annihilate pain *in futuro*, when its effects on the nervous system have entirely ceased? Ordinary sleep often produces a temporary loss of sensation of pain but this immediately returns in the waking state.

This announcement has a footnote appended reading as follows: "We have since learned from another quarter that the respiration of the vapour has been tried in numerous cases without occurrence of any accidents." This suggests that the editor of the *Gazette* had at first seen only the Jacob Bigelow letter and was subsequently shown the communication that appeared in the *Boston Daily Advertiser*.

The story of Boott's transmission of the Bigelow letter and the *Daily Advertiser* reprint to Robert Liston is well known, but the speed with which Liston verified the discovery has not been sufficiently emphasized. It appears that Liston was informed of Bigelow's paper some time on Friday, December 18, the day on which the *Gazette* appeared, on Saturday he obtained some ether, and on Sunday he worked all day trying to perfect an inhaler, which he tried out on his nephew William Squire*. On Monday, December 21, he carried out his celebrated amputation at the thigh—the first operation under ether anesthesia to be performed outside the United States. A few hours after the operation had been completed, Liston wrote Boott: "I tried the ether inhalation today in a case of amputation of the thigh and in another requiring evulsion of both sides of the great toenail, one of the most painful operations in surgery, and with the most perfect and satisfactory results." This Liston letter and the correspondence between Jacob Bigelow and Francis Boott and between Boott and Liston were all published in the issue of the *Lancet* previously mentioned, likewise reprinted was the full text of Henry Jacob Bigelow's communication

in the *Boston Medical and Surgical Journal*, as reprinted in the *Advertiser*.

On the editorial page of this number of the *Lancet* there is the following brief, but significant, comment:

In another page we insert an important communication kindly forwarded to us by Dr. Boott, of Gower Street, describing the important discovery of an apparently harmless means of producing insensibility during the performance of surgical operations. The means of performing operations without pain has, in all ages, occupied the attention of the profession. The realization of such an object, by means so simple as the inhalation of the vapour of sulphuric ether, cannot but redound to the great merit and reputation of the discoverer, Dr. Morton, of Boston, America; and to the honour of the profession to which he belongs. It is almost impossible to discredit the statement contained in the communication referred to, from which it will be seen that a great number of operations, from the extraction of teeth to the gravest operations of surgery, have been painlessly performed. This discovery seems to have a remarkable perfection about it, even in its first promulgation. We shall watch its development in the various branches of medicine and surgery which may admit of its application, and carefully record them. We suppose we shall now hear no more of mesmerism and its absurdities as preparatives for surgical operations. The destruction of one limb of the mesmeric quackery will be one not inconsiderable merit of this most valuable discovery. The operations of Mr. Liston, at University College Hospital, were performed after the inhalation of ether, by means of an apparatus contrived by Mr. Squires of Oxford Street. It appears, from a communication in another column, that the discovery has been patented for Great Britain and the Colonies.

The growth of interest in ether anesthesia in other countries was almost phenomenal for those days of slow communication, indeed, knowledge of anesthesia spread more rapidly on the continent of Europe† than it did in the United States, where the introduction of this new surgical concept was actively resisted in many centers, including New York, New Orleans and, particularly, Philadelphia. It is amusing, in retrospect, to find that that stately sheet the *American Journal of Medical Sciences*, so long edited in Philadelphia, refused throughout the year 1847 to publish a single original communication on anesthesia, although it did include, probably with reluctance, a few brief abstracts on the use of ether. The conservative *Lancet*, on the other hand, published nearly two hundred letters, communications, and editorials during 1847. An even larger number appeared during that year in the *Boston Medical and Surgical Journal*, and its successor, the *New England Journal of Medicine*, can now point with justifiable pride to having carried, one hundred years ago, the announcement of the greatest single discovery in the history of modern medicine.

333 Cedar Street

*Cock, F. W. First operation under ether in Europe story of three days. *Univ Coll Hosp Mag* 1:127-144, 1911.

†Accounts of the introduction of anesthesia in various countries of the world will be found in the "Anesthesia Number" of the *Journal of the History of Medicine and the Allied Sciences* (October 1946) and in the anesthesia numbers of the *British Medical Bulletin* (July 1946) and the *British Medical Journal* (Oct. 12, 1946). Attention must be directed, finally, to the new definitive history of inhalation anesthesia by Dr. Barbara Duncan (*The Development of Inhalation Anesthesia, with Special Reference to the Years 1846-1900*) just published for the Wellcome Historical Medical Museum in London.

FUNCTIONAL GASTROINTESTINAL DISORDERS LESSONS LEARNED FROM MILITARY MEDICINE*

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IT HAS long been customary to treat functional gastrointestinal disorders by means of smooth diets, antispasmodics, sedatives and rest. Hospitalization is sometimes recommended in severe cases. Experience in the management of soldiers with these disorders demonstrated that this type of treatment was not only unsuccessful in relieving symptoms but also harmful from a military point of view because it rendered the men unnecessarily ineffective as soldiers. The reason for this was that at least 80 per cent of the cases were psychogenic. Dealing with the personality disturbance directly and promptly, with a minimum of emphasis on medical study and organic therapy, resulted in a significant saving in manpower, a marked decrease in hospitalization and benefit to the patients. It is believed that the lessons learned in the study of soldiers with functional gastrointestinal disorders may be applied to the treatment of these conditions among civilian patients.

GENERAL CONSIDERATIONS

Functional gastrointestinal disorders accounted for a large part of disability from medical causes in the United States Army. The chief manifestation was epigastric distress or dyspepsia. In the British Army dyspepsia was, according to Hurst et al.,¹ the largest single type of disease. Regarding the incidence of peptic ulcer in relation to all cases of dyspepsia it is difficult to evaluate statistics, which are always conditioned by the type of hospital from which they are gathered. A study of the available sources of information indicated, however, that the incidence of ulcer among American troops was no greater than that in civilian life. Combat did not cause new ulcers to develop — less than 4 per cent of 183 consecutive patients with chronic epigastric distress in the Fifth Army who were completely studied were found to have peptic ulcer.²

Careful study of ulcer and nonulcer dyspepsia was made at the Sixth General Hospital in Casablanca and in a gastrointestinal center of the Fifth Army.³ Although the digestive symptoms of about a quarter of the patients with nonulcer dyspepsia superficially resembled those of ulcer, the personality types were nearly always totally unlike. This difference was so constant that a diagnosis could be made from the history alone with an accuracy of about 90 per cent. Psychiatric study of 100 patients in each group revealed that 80 per cent

of the nonulcer patients were psychoneurotic in the sense that they were rendered ineffective by neurotic symptoms in addition to the dyspepsia. In the ulcer group only 6 per cent had disability resulting from psychoneurosis. The personality make-up of the ulcer patient was that of a restless, ambitious person intensely anxious to succeed and to prove himself a leader. He was self-sufficient, self-reliant and usually an excellent soldier; he did not, characteristically, make use of his symptoms to get out of unpleasant situations — on the contrary, he often concealed his symptoms. The patient with functional dyspepsia, on the other hand, was generally an habitué of sick call, and typically was a submissive, passive person. Two fifths of these patients came from broken homes, and about half had a history of neurotic traits and phobias.

The clinical picture in the two groups was as a rule entirely different. In the functional group the main symptom was diffuse epigastric distress occurring while eating or immediately thereafter. Vomiting was frequent but usually consisted in regurgitation of a small amount of food after eating. Loss of weight was not evident. These patients, who rarely had diarrhea or large-bowel symptoms, nearly always complained of other symptoms, such as insomnia, lightheadedness, fatigue and headache. The patients often had lifelong dislike of certain foods, being extremely fussy about what they were able to eat. They were convinced that their symptoms were caused by the wrong food, but they rarely felt any better when given a bland diet in the hospital.

In contrast, the ulcer patient was nearly always relieved of symptoms as soon as he was hospitalized, even when good dietary facilities were not available. The symptoms were typical of ulcer, with a food-pain-food-relief sequence in 72 per cent of the cases. Vomiting was rare, and the patient generally complained of nothing more than localized epigastric pain. Characteristically, he did not complain about this unless asked.

The strikingly prompt relief of symptoms with hospitalization in ulcer patients seen overseas was attributed largely to relief of nervous tension, because in each case the soldier knew he was to be sent home with an acceptable organic disease, having done his job. Although nervous influences peculiar to Army life overseas did not result in an increased incidence of new ulcers, old ulcers were reactivated or intensified by nervous tension.² The subsidence of symptoms coincident with relief of nervous tension can be likened to that following vagotomy, when pain is likewise promptly relieved.

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In the former, hypersecretion and hypermotility are arrested, perhaps from cessation of vagal overstimulation by reducing psychic tension, and in the latter by surgical interruption of the vagal pathways from the higher centers to the stomach.

The proportion of ulcer patients with psychoneurotic symptoms is probably considerably higher in civilian practice than that in the Army overseas, because the overseas group was a highly selective one, neurotic patients with ulcer being much likelier to get themselves out of the Army than the aggressive ambitious type to which most of the overseas ulcer patients conformed. As a result of this selective process, it was much less frequent to find an association of neurosis with chronic organic disease in the Army overseas than in civilian practice. Thus, differential diagnosis was of great positive and practical value in estimating the personality of the patient.

At the Sixth General Hospital in Casablanca, a base hospital that was far back from the Tunisian front, the patients with functional dyspepsia had generally been in other medical installations for several weeks before they were received. When symptoms were vague or persistent and did not respond to treatment at forward hospitals, the patients were evacuated to the rear for investigation. When the symptoms were actually part of a psychoneurosis, hospitalization and repeated medical investigation rendered these patients less and less effective—62 per cent had to be returned to the United States, and a large proportion of those returned to duty were soon rehospitalized. An attitude on the part of the examining physician that led to exclusion of organic disease by all possible diagnostic tests before a neurotic etiology was accepted, even if there was positive evidence of neurosis, caused fixation of symptoms and magnification of the illness in the patient's mind. The patient with a psychosomatic syndrome, like every soldier, was in a conflict between duty and self-preservation. A prolonged search for organic disease apparently resulted in intensification of the neurosis by which the psychosomatic patient was solving this conflict.

Although prolonged investigation was harmful to patients with functional dyspepsia, it was not the investigative procedure itself that was harmful but the way in which it was carried out. Thus, if the history was taken only from the viewpoint of the gastric symptomatology and followed by x-ray and laboratory studies, with eventual evacuation of the patient to a rear hospital for further examination because the symptoms had not been relieved by treatment and because no physical cause had been found, the patient's mind was conditioned to organic disease, largely because the physician had manifested doubt regarding the diagnosis to the patient. When a decision was finally made in the rear hospital to return the patient to duty, it was

quite natural for him to feel resentful and to believe that the proper diagnosis must have been missed.

It seemed clear that if such patients could be evaluated promptly close to the front, a considerable saving in manpower would result. In 1943 in Italy, such an opportunity was provided by the establishment of a gastrointestinal center in the Fifth Army, at which all types of gastrointestinal disease were seen but the main diagnostic problem was the differentiation of ulcer and nonulcer dyspepsia. The patients were interviewed at length and a psychiatrist examined those in whom there was doubt concerning the diagnosis. If the symptoms were believed to be psychogenic, the patient was so informed. X-ray facilities were not at times adequate, although in doubtful cases x-ray examination could be done. As a result of complete studies previously carried out in a similar group of patients at the base hospital, it was believed the ulcer could be eliminated from the history with a high degree of accuracy. When the study of the patient was completed, a decision whether or not he was fit for further duty was made chiefly on the basis of psychiatric factors. He was then again interviewed, and the mechanism of symptoms, as well as the decision regarding his disposition, was explained to him. Treatment of the stomach symptoms by means of rest, diet and medicine, which was invariably fruitless, was not attempted, since in itself such treatment was unsettling to the neurotic patient. The symptoms, being a manifestation of anxiety and personality disturbance, could not be cured by medicine. Although malingering was rare, there was usually an unconscious exaggeration of symptoms.

As a result of this method of management, the patients felt confidence from having been taken seriously and having been well examined. Under these circumstances, they returned to duty quite willingly, for they still retained their sense of unit morale, not having been separated from their unit for more than a week.

The results of this system were militarily beneficial. 80 per cent of patients with functional dyspepsia were returned to combat duty, and about 10 per cent were reclassified for noncombat duties in other organizations, in about 10 per cent of cases either the patients were too sick psychiatrically for any type of duty or there was sufficient doubt regarding the diagnosis to warrant evacuation to a rear hospital. A follow-up study of those returned to duty two to four months later demonstrated that 83 per cent were still on duty and that 68 per cent of these were considered effective as soldiers by their officers. The contrast between these figures and the results obtained when the patients were hospitalized for long periods, as at Casablanca, is striking. Even though the neuroses of patients in the Casablanca group were severer than those in the Fifth Army group, there was no

doubt that unnecessarily prolonged medical investigation played a major role in the unsatisfactory results. Although the Fifth Army patients were all combat soldiers, the symptoms were not merely a reaction to combat, since 68 per cent had had symptoms in civilian life. The system of early and prompt treatment and disposition was beneficial to the patient individually, by preventing perpetuation of symptoms. It was therefore sound preventive medicine.

The Army setting was an artificial one in comparison with civilian practice in that neurotic patients with a chronic organic disease were apt to be screened out before they were sent overseas. Furthermore, the patients were all young men living under nearly identical conditions. It provided an experimental situation, however, in which observations could be made more precisely than in civilian clinics. Thus, the effect of nervous influences associated with combat could be studied in relation to peptic ulcer, and the adverse effect of ill-advised medical investigation on psychosomatic conditions could be demonstrated with precision. It is now necessary to determine whether these observations can be applied to the treatment of functional gastrointestinal disorders in civilian practice.

The clinical picture differed in the Army from that seen in civilian practice. Dyspepsia and epigastric symptoms predominated, patients with large-bowel symptoms of colicky pain, constipation and intermittent diarrhea being quite rare. In World War I neurocirculatory asthenia, or soldier's heart, was the major psychosomatic syndrome. Although that symptom was not infrequent in World War II, dyspepsia, or "soldier's stomach," as it has been termed, seems to have taken its place as the main psychosomatic disorder. The symptomatology, outlined above, was so uniform that it seemed at times to assume epidemic proportions. The factor of suggestibility in neurotic patients may have been the reason for the uniformity in symptomatology.

In civilian practice patients with functional disorders seem to have much more varied symptomatology, large-bowel syndromes predominating. Furthermore, the majority of patients are women, and they are in older age groups. The fundamental etiologic factors, however, are apparently the same.

ETIOLOGY

There are four main explanations for a functional gastrointestinal disorder. It may be associated primarily with an organic disease, such as tuberculosis or nephritis or with the menopause. It may occur in a perfectly normal person subjected to unusual physical or emotional strain — in such cases it is temporary, being relieved when the external circumstances causing the strain are corrected, and is essentially physiologic. It may occur in emotionally stable

persons who seem to have a low threshold for gastrointestinal symptoms that are precipitated by external influences that do not affect the average person, mild fatigue, normal fear, nicotine, alcohol, certain foods and irregular eating habits are examples of such influences. Finally, the disorder may be part of an emotional disturbance or neurosis, often masking other symptoms of the neurosis so that on superficial examination dyspepsia, pain, heartburn, vomiting and so forth seem to be the only difficulties.

The physiologic mechanism responsible for symptoms is not completely understood, but disturbance in motility appears to be the essential feature. Measurement of gastric secretion is without value in assessing the etiology of symptoms, since the same symptoms may occur whether or not hyperacidity, anacidity or normal acid values are present. Changes in vascularity probably play a secondary role in the production of gastric symptoms. Wolf and Wolff⁴ demonstrated that stimulation of the normal gastric mucosa resulted in no sensations but that when the mucosa was turgid and edematous the same stimulation produced symptoms. In connection with motor phenomena, a word should be said about pylorospasm, which has long been considered the origin of symptoms in many cases of dyspepsia, often being said to be a pathologic entity. Evidence for pylorospasm is by inference, being based chiefly on roentgenography when the pylorus fails to open to allow barium to pass through. Recent studies suggest that there is no such thing as pylorospasm, except in ulcer or adjacent inflammatory disease.⁵ The failure of the pylorus to open may be due not to spasm but to absence of peristaltic contractions sufficiently strong to cause it to open. Spasm may occur in the body of the stomach, however, being frequently observed at gastroscopy. In gastroscopy of 110 soldiers with nonulcer dyspepsia spasm was noted in the mid-body region of the stomach in 7 cases.⁶ In 2 of these cases the patients stated that an exact reproduction of their usual symptoms took place at the time the spasm was noted. The gastric mucosa was normal in both cases.

TREATMENT

Regarding treatment, it is first necessary to determine which of the four fundamental causes of the disorder is the basis of symptoms in the patient. If the disorder is primarily associated with external factors, such as overwork, improper food and overindulgence in tobacco, the approach to the problem is essentially an organic one — that is, the emphasis is on rest, diet and drugs. On the other hand, if emotional tension or psychoneurosis is the basic difficulty, the treatment should be primarily psychiatric. Bed rest, diet and drugs in the treatment of neurosis, unless used merely as temporary adjuncts to psychotherapy, are harmful because

they tend to perpetuate the neurosis, making subsequent psychotherapy more difficult. Menninger⁷ has pointed out the reasons why neurotic patients uniformly demand physical treatments and resist facing underlying emotional factors: they always prefer to have a physical rather than a mental illness, and physical treatment justifies the patient's desire and belief that he should be considered physically ill. Bennett⁸ has made a study of 150 patients on the medical and surgical wards of a general hospital whose complaints were eventually diagnosed as psychoneurosis. A large proportion had gastrointestinal symptoms, four hundred and ninety-six courses of medical and two hundred and forty-four courses of surgical treatment had previously been conducted, never with more than temporary benefit. Such fruitless therapy involves enormous waste of time and money and tends to encourage reliance on cults, with loss of confidence in the profession.

The treatment of functional gastrointestinal disorders in soldiers was in a sense a negative one. The patient could only be told what the trouble was and that he would have to live with it. The environment could not be altered, nor could sources of frustration, resentment or anxiety be eliminated. Delving deeply into the background of the patient in an attempt to alter basic difficulties was unsuccessful and unwise—one patient in whom this was attempted developed marked mental anxiety, and another developed hysterical paralysis of a limb. In civilian practice external factors can be altered. Compromises, adjustments and a changed viewpoint can be effected. Because there is a greater incentive to get well, simple psychotherapy may be successful, especially if carried out early before harmful measures that strengthen the neurosis have been applied.

In functional illness the process of making the diagnosis is in itself an effective therapeutic measure. Even though the physician is sure after five minutes' conversation that the disorder is functional it is imperative that a thorough history be taken, a thorough examination made and essential laboratory and x-ray studies carried out. It is important, however, that these investigations be performed but once and that after this systematic examination is made the physician speak with conviction and positiveness. The most valuable part of the examination is the history, which may disclose positive evidence of emotional instability. Such a positive finding is as essential to the diagnosis of a psychogenic disorder as x-ray evidence is to the diagnosis of peptic ulcer. It must not be a diagnosis of exclusion. The physician need not have psychiatric training to recognize emotional factors, but he should have the experience to appreciate that they may produce major physical discomfort. If one embarks on an unreasonably prolonged search for organic disease or picks an incidental finding, such

as a spastic colon, treating the patient as if that were in itself a disease entity, the patient will become convinced that he is organically ill. Such treatment, however, often results in temporary symptomatic relief at least during the time that the patient is under the physician's care, in contrast to soldier patients, in whom it was rarely beneficial.

In functional gastrointestinal disorders caused by distant organic disease or by external strains in a normal person, the treatment is obviously that of removing the causes. In those due to external strains in a patient with a low threshold for gastrointestinal symptoms, the patient must be taught his limitations and how to adjust his life to them. Antispasmodics, a simple diet and adequate rest are of considerable help.

It is in the group with psychogenic symptoms that therapy is the most difficult. Since this comprised four fifths of the soldier patients, it is reasonable to suppose that it is the largest group in civilian practice. The greatest obstacle is the factor of time. Most physicians do not have enough time to deal thoroughly with a psychogenic disorder. It is difficult to persuade patients with a psychosomatic syndrome to consult a psychiatrist, for the essence of this type of disorder is the patient's resistance to accepting the fact that the symptoms are emotional in origin. A trap is therefore set by which symptoms may become fixed. The patient wants organic therapy, and owing to the physician's lack of time, it is easier to give it than to spend a few hours dealing with the patient's problems.

If psychogenic gastrointestinal disorders were correctly diagnosed and properly treated at the beginning, much subsequent disability and invalidism could undoubtedly be prevented. In the first stages simple measures are often successful without the expenditure of a great deal of time.

In brief, the first step is to explain clearly that although the symptoms are not caused by any physical abnormality, they are real. Nearly always the patient fears that the doctor considers the symptoms imaginary. A physiologic explanation of symptoms is helpful, with a description of how exaggerated nerve impulses resulting from tension or anxiety travel to the intestinal tract and cause spasm, which produces distress. Often the patient asks whether these abnormal conditions may lead to cancer or ulcer, and reassurance is necessary on this point alone. Reassurance that the patient has nothing seriously wrong, however, is in itself of little value. A positive statement by the physician that the patient will feel better and that he can get well often has a marked therapeutic effect. If this has been preceded by a thorough clinical examination, it may be one of the most potent forces in therapy. Explanation, reassurance and suggestion by themselves are generally not enough and should be reinforced by the support of the physician, who

must give the patient advice how to adjust himself to difficult situations and try to make the patient see how situations that produce nervous strain are often followed by symptoms. The tendency of the patient is to say that nervousness is caused by the symptoms. If the patient can be made to understand that emotional difficulties are actually causing them, he will be a long way on the road to solving these difficulties himself.

In purely psychogenic disorders a bland diet, antispasmodic drugs and mild sedation with phenobarbital all have a place. Doubtless these agents at times have both a physiologic and a pharmacologic action, but it may be seriously questioned whether the beneficial results attributed are not usually those of suggestion — a symbol of the doctor's authority. Certainly the patient will welcome such treatment, and in some cases it may be given at the start. The patient should be told emphatically, however, that this is given only for the secondary manifestations and will not affect the cause of his difficulty. Because the patient frequently improves, it is a temptation to continue a medical regime indefinitely. This practice is basically unsound, being harmful by creating the belief that the symptoms are of physical origin.

Of course, in a great many patients who are confirmed gastrointestinal invalids, simple common-sense psychotherapy is of no avail. These patients demand diet ceremonials, vitamins and other medicines and resist any attempts to explain their symptoms on an emotional basis. Few accept the suggestion that they see a psychiatrist, and it is indeed probable that expert psychotherapy would not cure many patients in whom the symptoms are firmly fixed. It seems likely that much of this invalidism is largely caused by injudicious medical therapy at the beginning and that a better understanding of functional illness, with treatment of

basic causes rather than the organ involved, can prevent much future disability.

SUMMARY

Men with functional gastrointestinal disorders formed one of the largest single groups of medical patients in the Army Hospitalization, with prolonged investigation and medical treatment, had an adverse effect because the great majority of the disorders were psychogenic. Prompt evaluation, with early discharge from medical channels, resulted in military benefit by preventing perpetuation of symptoms.

The personality of soldiers with peptic ulcer seen overseas differed markedly from that of patients with nonulcer dyspepsia. This observation was useful in differential diagnosis, being of practical value in forward areas, where x-ray facilities were not always available.

In civilian patients with psychogenic gastrointestinal disorders, treatment with diets, drugs and other forms of organic therapy, unless used as a temporary adjunct to psychotherapy, may be a major cause of disability and invalidism by fixation of symptoms.

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MEDICAL ASPECTS OF HYPERTENSION*

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HYPERTENSION, with its allied circulatory disorders, is probably the most frequent single abnormal medical condition seen in practice. There are believed to be about 15,000,000 people in the United States with some degree of hypertension. These cases are usually divided into those in which the hypertension is a manifestation of some specific disturbance of the body, such as nephritis or hyperthyroidism, and those in which it is the sole abnormal finding on examination, or in which other findings existent at a particular time are presumed to have been secondary to an earlier essential hypertension. In a discussion of this sort it seems feasible to ignore cases in which the abnormally high pressure is secondary to other diseases because the main consideration in such cases is the investigation and treatment of the primary disorder.

Essential hypertension has long been an enigma to the clinician, and vast amounts of energy and money have been expended in a search for the causative factors, that more effective preventive and therapeutic measures might be developed. The work of Goldblatt¹ on the effect of renal ischemia on blood pressure served to focus attention on the results of slowing down the circulation to one kidney. One practical effect of the publication of this material has been our routine search for unilateral kidney lesions as a cause for hypertension. At times, spectacular remissions have occurred with correction of such a remedial condition as a unilateral congenital poorly functioning kidney.

Subsequently, the work of Page and his associates²⁻⁶ indicated that the kidney liberates into the blood stream a proteolytic enzyme (renin) that acts on a blood globulin to produce a polypeptid with a pressor effect — angiotonin, or hypertensin. Experimental renal ischemia has been reported as producing an increase in circulating renin and angiotonin,⁷⁻¹⁰ and the same results are said to occur in eclampsia and severe glomerulonephritis.¹¹ The assumption, however, that a deficient renal circulation produces essential hypertension by the increased elaboration of renin and angiotonin was upset by the demonstration that renin is not found in the blood in essential hypertension,¹² although it is present in renal hypertension and severe glomerulonephritis. Nor is there any increase in the globulin precursor of angiotonin in essential hypertension.¹³

A further accumulation of doubt regarding the role of a humoral pressor mechanism arose with the demonstration that repeated transfusions from

hypertensive subjects did not cause blood-pressure elevation in the recipients.¹⁴ It was also demonstrated by several investigators that renal blood flow in essential hypertension is normal,¹⁵⁻¹⁸ so that there appears to be no evidence of renal ischemia in the genesis of this condition. It may be said that the excellent work of Goldblatt has resulted in a tremendous amount of clinical investigation, some of the results of which were aptly expressed by Smith and his co-workers¹⁹ as follows: "So far as the genesis of essential hypertension is concerned, the kidney appears to be the victim rather than the culprit." Page's^{20, 21} confirmation of this statement is borne out by his conclusion that there is little evidence that persistent reduction of blood flow and oxygen utilization occurs within the kidneys except when hypertension is of long duration and severe secondary vascular change has supervened.

Circulatory interference with other tissues has been advanced as a cause of arterial hypertension. The recent and as yet unfinished investigation of Victor and his associates²² revealed a marked, persistent increase in blood pressure in six dogs in which ligation of the left adrenal vessels was carried out. A theory that hypertension is caused by excitation of the vasomotor center as a result of the ischemia associated with arteriosclerotic changes in the small vessels of the medulla²³ does not seem to have been borne out by the pathological findings of others, including Cutler.²⁴

The neurogenic theories of hypertension are rapidly replacing those having to do with a renal etiology. The reactions of the vasomotor center are influenced by such factors as carotid-sinus reflexes, oxygen and carbon dioxide tension, medullary circulation and certainly by nervous and emotional states. According to Donnison²⁵ and Williams²⁶ hypertension is rare in the African Negro but is frequently seen in the Negro in metropolitan areas of the United States.^{27, 28} The influence of psychosomatic factors in elevated blood pressure has been mentioned by a number of authors.²⁹⁻³³ Everyone who has had occasion to treat hypertension has noted the result of psychogenic influences on some patients. The effect of inhibited, excessive, competitive and hostile reactions on the blood pressure is well known to every physician. Similarly, the favorable response incident to the control or elimination of such hypertensive stimuli is common knowledge. The persistent occurrence of such mental states and the knowledge of the beneficial effects obtained by their proper handling have led to the frequent usage of various sedatives. The continuation of this therapy is assured by an

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increased observation of the neurogenic factor in hypertension, and by a firm belief that sustained vasomotor stimulation caused by such nervous and emotional influences eventually leads to fixed hypertension—an assumption that is lent great weight by the report of Levy, Hillman, Stroud and White³⁴ on the occurrence of transient hypertension in a large group of United States Army officers. They found evidence that at all ages, sustained hypertension developed oftener in persons who had previously shown transient hypertension than in those who had not.

Many years ago, Dr. James P. O'Hare pointed out to me that the early stage of essential hypertension may be characterized by intermittent elevations of pressure followed by remissions to normal. He also concluded, after long observation of a large number of hypertensive patients in the clinic and in private practice, that a certain number are not particularly troubled by essential hypertension, living through what appears to be for them a normal span of years and then dying of some extravascular disorder. Recently, concentration on the neurogenic element in hypertension has resulted in recourse to surgical therapy in some cases. It is to be hoped that the pendulum will not swing too far in that direction, and yet there is some suggestion that it has already done so. The recommendation sometimes made that young persons in the early intermittent or transient stage of hypertension be subjected to surgery hardly seems justified in view of the knowledge of the normal life expectancy of a certain percentage of such a group. Peet and Isberg³⁵ have pointed out that the acceptance of surgical treatment has been tempered with the realization that its limitations are definite and that failures are not infrequent. No one can review such a report without recognizing the distinct value of the surgical procedure that is advocated in certain selected cases. That there is difficulty in choosing the ideal case for surgery is readily admitted, but I believe that rapid strides are being made toward the solution of this troublesome problem.

Various procedures have been used to determine the lability of the blood pressure in a particular case and in this way to set up criteria for the selection of suitable operative cases. The proper determination of operability is of great importance to the internist, who is often the one to make the surgical recommendation. If the results of such therapy are universally poor, a valuable procedure may fall into disrepute and may thus deprive some patients of increased comfort and prolonged life. The sodium amytal, sodium nitrite and cold-pressor tests are still used routinely as part of the investigation into the degree of neurogenesis in essential hypertension. The failure of these tests accurately to prophesy success for sympathectomy in some cases indicates the need for a more effective evaluating mechanism.

The recently published studies of Russek, Southworth and Zohman³⁶ on the use of continuous caudal anesthesia as a means of selecting hypertensive patients for surgery suggests that this procedure offers a valuable indication of the success or failure of sympathectomy. Unfortunately, there is no evidence regarding how long these patients were followed postoperatively. The assumption that it may be possible to correlate the level of anesthesia necessary for a satisfactory fall in blood pressure with the extent of surgery required for relief is certainly interesting and indicates the progress that may well be made in arriving at a proper surgical evaluation.

It is worth remembering that in many cases in which surgery has failed to alter the blood-pressure reading materially, a favorable influence has been exerted on distressing symptoms. In the series reported by Bartels, Poppen and Richards³⁷ 71 per cent of patients received symptomatic relief, although half continued with an elevated pressure. Similar results are frequent in other case series. It hardly seems justifiable at present, however, to recommend such a serious surgical procedure purely for the temporary relief of symptoms.

The classification of patients according to fundoscopic changes and alteration of cardiac and renal function is certainly most desirable as a means of measuring the progress of a vascular disease. An adequate period of careful observation may well result in presenting to the surgeon at a more favorable time the occasional case in which sympathectomy will be beneficial.

From the standpoint of the internist and the general practitioner it is obvious that the most useful type of treatment is that afforded by psychotherapy, particularly in the form of reassurance, and by the time-honored use of sedatives that offer additional reassurance by lessening nervous tension and promoting sleep. Far too many people in this section of the country are blood-pressure conscious, and yet such a state of mind is beneficial from the standpoint of preventive medicine because it enables the physician to steer these people along a better nervous and emotional course. In this way he is able to remove early some of the vasospastic element that might conceivably contribute to vascular change and a speeding of the patient along the road to permanent fixed hypertension.

I remember two young women who were strongly urged to subject themselves to sympathectomy because of transient hypertension, obviously related to sleeplessness and worry. Neither has shown an elevation in the blood pressure for some time, one having gone four and a half years without symptoms and with a blood pressure of 136 systolic, 90 diastolic, as compared with an original reading of 162 systolic, 100 diastolic. The only therapy has been reassurance and limited sedation.

I am still of the opinion that iodides are valuable in the treatment of vascular diseases, including

hypertension. Similarly, the nitrites are useful in some cases because of their antagonistic effect on vasospasm. O'Hare et al.^{38, 39} have shown the dramatic effect of thiocyanate therapy in selected cases of hypertension in which the dosage was carefully regulated by determination of the blood cyanate levels. A few years ago there was high hope for the commercial development of a renal extract with an antipressor effect, but such a product has not yet been assured.

* * *

In conclusion, I should like to make a sincere plea that the fundamental treatment of essential hypertension be continued on a conservative basis, and that these patients be given every advantage of study over a reasonable period, so that the progressive or regressive character of their conditions may be accurately determined. This approach to an important problem will undoubtedly assure many of these patients a normal life expectancy, and will place in the hands of the surgeon at a more opportune time patients who will probably be benefited more specifically by sympathectomy.

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Correction. In the paper "Some Unusual Findings in an Epidemic of Anterior Poliomyelitis," by Major Joseph H. Nicholson, which appeared in the August 15 issue of the *Journal*, the asterisk following the title should be deleted. The footnote refers to the asterisk in the text.

MEDICAL PROGRESS

BIOCHEMICAL ABNORMALITIES DURING RENAL INSUFFICIENCY*

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DURING recent years the theory of metabolism has undergone an extensive revision as a result of the work of Borsook and Keighley,¹ Tarver and Schmidt,² Schoenheimer³ and others. This new point of view, summarized by Schoenheimer, has had a profound influence on thinking in biochemistry and physiology. In particular, it has been necessary to reassess the part played by the kidney in the body economy and to reconsider — in terms of the organism as a whole — the biochemical abnormalities that arise during renal insufficiency.

According to modern theory, the components of the body are in a state of continual change. Thus, the constancy of any biologic structure does not imply stability, but denotes a balance of the processes of degradation and regeneration in which its ingredients participate. Complex molecules of all types break down or lose molecular groups and are again rebuilt or regain lost groups. This intricate and cyclic activity takes place in a circulating so-called "metabolic pool," in which small molecules derived from degradation or digested food are carried throughout the body. Likewise, the mineral constituents of cells and body fluids are in dynamic equilibrium, undergoing continuous movement and exchange.

It is obvious that the position of the kidney in this activity is extremely important, since it governs the composition of the metabolic pool through its regulation of the chemical structure of the plasma, although the factors involved are obscure.⁴ It is equally probable that the kidney acts to maintain the constancy of some single plasma characteristic, such as ionic strength, osmotic pressure, water, base or hormone content or the constancy of several. In any case, the net result is a remarkably small range of variation in the composition of the plasma under diverse conditions. Since the plasma is in equilibrium with the remainder of extracellular fluid, which, in turn, is in equilibrium with intracellular fluid in most respects, it follows that renal activity determines the structure of all body fluids making up the metabolic pool.

Although many biologic processes are, to a large extent, independent of the composition of the metabolic pool, it seems certain that extensive changes, such as those occurring during renal insufficiency,

may disturb chemical reactions everywhere in the body and ultimately lead to fatal dislocation of the metabolic balance. According to this view, it is gratuitous to seek an explanation for the clinical manifestations of uremia in the renal retention of specific toxic waste products. Any great loss of water and electrolytes, with a retention of catabolites by the damaged kidneys, is sufficient to provoke serious disturbances of cellular activity, with resultant clinical phenomena. Thus, a study of the chemical structure of the blood during renal disease reveals not only the effects of renal dysfunction on body fluids, but also the causes of cellular dysfunction elsewhere in the body.

The failure of the renal mechanisms that normally regulate the composition of the blood — that is, renal insufficiency — arises from a wide variety of disorders and produces an equally varied pattern of chemical change. These alterations depend on the compensatory activities of various extrarenal mechanisms, the presence of complicating factors, such as infection and anemia, and the activity and diet of the patient, as well as on the character and extent of the renal lesions. Hence, it is extremely difficult, if not impossible, to relate specific renal structural alterations to distinctive chemical patterns. It is more convenient to consider the behavior of various substances in the blood during renal insufficiency and to discuss the implications of this behavior.

ELECTROLYTES

The modern dynamic theory of metabolism has developed in the course of studies of the fate of large organic molecules in the body, but a similar point of view regarding mineral metabolism has been widely held for many years. Recent work with isotopic tracers has served to strengthen this view.⁵ Electrolytes within the tissues and in the extracellular fluids are readily exchangeable. Indeed, an active exchange of ions is in continuous operation. The notion that the electrolytes of the cells and extracellular fluid are held apart by more or less rigidly semipermeable membranes is no longer tenable.

This idea has been based on the fact that the electrolytic structure of the plasma and extracellular water differs from that of the intracellular fluid. Sodium and chloride are present in higher concentrations than any other ions in the extracellular

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space, whereas potassium and phosphate predominate within the cells. The factors that determine these inequalities of ionic concentrations are obscure. Certainly, there is a demonstrable equilibrium between the ions of the two spaces, a change in the concentration outside the cells provoking a change within. In general, it appears that these changes are most important when alterations of the hydrogen ion concentration and osmotic pressure of the extracellular fluids occur.

Hydrogen Ion Concentration

One of the most carefully adjusted constants of the extracellular fluid is the hydrogen ion concentration^{4, 6-8}. This value is maintained within narrow limits just on the alkaline side of neutrality largely through the activity of buffer salts. These compounds react with strong acids or bases to produce neutral salts and weakly ionizable acids or bases. The carbonic acid-bicarbonate buffer is of special importance. It possesses a remarkably wide buffering capacity, since carbonic acid is easily and quickly excreted through the lungs. Acids other than carbonic acid and all bases must be excreted by the kidney. When renal dysfunction leads to an accumulation of acids or bases in the plasma, a significant change in the hydrogen ion concentration of the plasma ultimately occurs. Under these circumstances more slowly acting secondary measures of defense are brought into play, such as the mobilization of base fixed in bone and the movement of phosphate into the cells. During acid-base imbalance of sufficient magnitude and duration, the compensatory adjustments may, in themselves, prove harmful, producing respiratory abnormalities or malformation of bone. Thus, efficient renal control of hydrogen ion concentration is vital, and when interfered with by disease, may not be readily corrected by extrarenal mechanisms.

The renal regulation of the sodium concentration in the plasma is of major importance in the maintenance of acid-base balance. Since sodium constitutes approximately 95 per cent of the cations of plasma, it plays a prominent role in the establishment of the hydrogen ion concentration. A large number of sodium ions pass through the glomerular filter bed each minute, but active tubular reabsorption prevents the escape of many into the urine.⁴ This activity appears to occur chiefly in the proximal segments of the tubules.

The removal of sodium salts from the glomerular filtrate by tubular reabsorption would be expected to cause alterations in the reaction of the filtrate if reabsorption of the individual members of different buffer pairs were disproportionate. As a matter of fact, it has been held for many years that activity of this character is sufficient to account for urinary acidification or alkalization. According to one view,⁹ the hydrogen ion concentration of the urine is a function of the tubular reabsorption of

sodium bicarbonate. The chief weakness of this hypothesis lies in the assumption that tubule cells are impermeable to carbonic acid, a substance known to penetrate most cells with great ease.⁴ Another theory^{10, 11} places emphasis on the monosodium-disodium phosphate buffer pair, postulating that the monosodium species is reabsorbed selectively under conditions of alkalosis, with subsequent excretion of large amounts of sodium as the disodium salt. In acidosis the reverse is believed to occur. It may be noted that both hypotheses stipulate that all the hydrogen ions available for excretion must be present in the glomerular filtrate. The kidney tubules may then manipulate it as the situation demands. Pitts and Alexander¹⁰ have found that only about 30 per cent of the hydrogen ions excreted during acidosis could be accounted for on the basis of filtration alone. Hence, they concluded that hydrogen ions must be excreted actively by the tubule cells, a conclusion Smith¹ had reached, on theoretical grounds, in 1937.

The important study by Pitts and Alexander,¹⁰ indicating that the kidney can conserve a large amount of base by the simple expedient of exchanging hydrogen ions for sodium ions, has succeeded in clarifying, to a certain extent, the mechanism by which the exchange is effected. It is known that the kidney contains a high concentration of carbonic anhydrase, in common with the red cell, pancreas and gastric mucosa.¹² The ready availability of carbonic acid in tissues for the donation of hydrogen ions suggested that carbonic anhydrase might be concerned in the activity of making hydrogen ions more easily obtainable from this source. This chain of logic was completed by the finding that the administration of sulfanilamide, a well known carbonic anhydrase inactivator, was followed immediately by a markedly diminished secretion of hydrogen ions despite the presence of acidosis. It is possible that a similar inactivation occurs during renal insufficiency. The results of study in this direction should be of great interest.

A second, more slowly acting device by which the kidney reduces loss of base in the urine during the excretion of acidic ions, has been known for a long time and has been found to be deranged during renal insufficiency.¹³ This is the renal synthesis of ammonia and the replacement of cation by ammonium, the manner in which this mechanism is disturbed is unknown, although it appears, like the secretion of hydrogen ions, to involve interference with an enzyme system. For many years it has been widely believed that ammonia is derived from the hydrolysis of urea in the kidney¹⁴ and that the urea clearance requires correction on the basis of urea lost in this activity. A considerable amount of work has cast doubt on this belief. Previously, the major argument for the view was the reciprocal relation between urea and ammonia excretion, which is apparently fortuitous.¹⁵ In addition, only a

negligible amount of isotopic nitrogen derived from urea appears in urinary ammonia, whereas isotopic nitrogen placed in any amino acid appears soon after its administration in high concentration in the urinary ammonia.³ Thus, it seems certain that ammonia is derived from the deamination of amino acids in the renal tubular cells. Van Slyke and his associates¹⁸ recently found that approximately 60 per cent of the urinary ammonia arises from the plasma amino acid glutamine, which is broken down to ammonia and glutamic acid by the enzyme glutaminase. The remainder of the ammonia is derived from other plasma amino acids. The formation of ammonia begins slowly, some time after the establishment of a demand, in terms of excess acid for excretion, and once inaugurated continues for a short time after the need for it has vanished.^{7, 17} A considerable saving of base is effected through this process, amounting under extreme conditions of acidosis to about 75 per cent of the acid cleared.¹¹ The failure of the tubular cells to manufacture ammonia during renal insufficiency may indicate a loss of cells concerned in this activity or enzyme inactivation.

Acidosis usually develops at some time in the course of nearly every case of renal insufficiency.¹⁹ Rarely, no abnormality of the acid-base balance occurs, and even less often, an alkalosis develops.¹⁹ There is no typical pattern of electrolyte change that produces these states. In fact, almost any conceivable arrangement of electrolyte concentrations may appear, not only in different persons but also in the same patient at various times during the course of chronic renal failure. The retention of anions, such as chloride, sulfate, phosphate and organic acid radicals, may contribute to the acidosis, but the loss of base, largely sodium, because of the failure of base-saving mechanisms, accounts for the usual reduction of the carbon dioxide combining power. When chloride accumulation occurs it is often the result of overenthusiastic treatment with isotonic saline solution, since chloride ions are present in normal saline in higher concentration than in the plasma.²⁰ On the other hand, the loss of chloride may be excessive, causing evidence of alkalosis together with signs of peripheral circulatory collapse due to the loss of fluid with the chloride.²¹ Alkalosis during renal insufficiency may also follow excessive loss of chloride in vomitus.¹⁹ Usually, however, vomiting leads to an equivalent loss of base, since gastric secretion of acid is reduced in uremia.²²

Sodium, Chloride and Osmoregulation

The behavior of sodium, chloride and water in the body cannot be discussed separately, since the fate of each is intimately related to the destiny of the others.^{4, 6-8, 23, 24}

In the normal state both sodium and chloride are confined for the most part to the extracellular space.

Nevertheless, the small concentration of sodium within the cells may play a role in the support of the extracellular fraction, since the total bulk of the cells permits them to hold a significant quantity of sodium.²⁵ Chloride is almost entirely extracellular, although it moves in and out of the red cell with ease. Bone contains about a third of the sodium of the body in its interstitial spaces.⁸ This base is available for use in combating salt loss and deficiency, but it is primarily of value in disorders of prolonged duration, such as renal insufficiency, since its mobilization is relatively slow.

Water, of course, is distributed throughout the body tissues, but the proportional distribution is a function of the osmotic pressures in the intracellular and extracellular compartments. The osmotic pressure of extracellular fluid is largely a function of the concentrations of sodium and chloride, whereas that within the cells is determined by the concentrations of potassium, phosphate and protein.

The factors regulating the osmotic equilibria between cells and interstitial fluid are obscure. Two processes of adjustment have been elucidated. The first, chiefly important from the standpoint of the magnitude of the change it can buffer, is the transfer of water between the cell and the fluid surrounding it. It appears that the movement of water out of the cell compensates for increased tonicity of extracellular fluids, so that the final total change is about half what it would be in the absence of such a fluid shift. Hypotonicity leads to a reverse effect.²⁵ A second compensatory mechanism resides in the apparent ability of protoplasm to control the osmotic pressure of intracellular fluids by altering the ionization of intracellular electrolytes and, perhaps, by changing the configuration of intracellular proteins so that they exert more or less osmotic pressure as the occasion demands.²⁵

Shifts of electrolytes as well as of water may occur. The movement of electrolytes appears to become of importance when osmotic dislocations are large or prolonged. This shift seems definitely to occur under these conditions without the destruction of tissues. Since the total amount of sodium held in the cells is of significant magnitude, the movement of sodium from the cells into the extracellular fluid, together with some potassium, may be valuable in combating hyponatremia and acidosis. On the other hand, it has been found that alkalosis with excess base in the plasma may lead to the transfer of sodium into the cells.^{27, 28}

The factors that determine the distribution of water and electrolytes between the various subsidiary divisions of the extracellular fluid—plasma, interstitial fluid and the like—have been extensively studied.²³ Again, a balance of forces, tending to attract water into the plasma on the one hand and to drive it out on the other, is involved that may be seriously disturbed by renal insufficiency. In addition, such major determinants of water ex-

change as thirst, body temperature regulation, rate of gastrointestinal secretion and arterial pressure depend on equally exquisite balances that may be disturbed by renal disease

The renal excretion of water, sodium and chloride are closely related.⁴ Sodium is conserved or disposed of by the kidney by the processes described above. The tubular cells appear to reabsorb sodium as an independent substance, but the demands of ionic equilibria make this most complicated. In the urine, as in the blood, chloride is the chief anion associated with sodium, but the relative proportions may differ widely. Excessive excretion of sodium carries an excess amount of chloride ion out of the body with it, and the reverse is true. There is no threshold in the ordinary sense, for sodium and chloride are reabsorbed in variable amounts at any plasma level, depending on the requirements of the total body economy. Water is reabsorbed throughout the length of the tubule—in the proximal segment, in association with the reabsorption of various solutes, and in the distal segment, against an osmotic gradient.

Reabsorption of water and salt depends, in the main, on the state of the plasma flowing through the kidney, the amount of material reaching the tubules for reabsorption via the glomerular filtrate and the activity of various endocrine organs.

The first factor is of undoubted importance, since the structure of the plasma is, in the last analysis, the chief stimulus to which the kidney is subjected and under which it is moved to function in various directions. Just how this stimulus works is almost entirely unknown. Certainly, a deficit or excess of sodium or chloride in the plasma quickly elicits greater or less activity of the tubule cells in withdrawing these substances from the filtrate even when there is no added stimulus in terms of acid-base imbalance. Likewise, it has been shown that a factor of plasma concentration operates in determining the renal reabsorption of water.²⁹

The second factor is somewhat more accessible to study with the available technics. Two aspects of this activity require consideration. First, the character of the filtrate is essential in determining reabsorptive activity. When substances such as potassium, sulfate and glucose appear in the filtrate in higher concentrations than normal, a diuresis results in which an excessive amount of sodium, chloride and water is lost. Secondly, the relation between the volume of glomerular filtrate and the capacity of the tubules to handle it is significant, particularly in pathologic processes that may interfere with the normally prevailing balance.³⁰ Reduction of filtration without concomitant reduction of tubular capacity, as in acute diffuse glomerulonephritis, may result in excessive reabsorption of water and electrolytes, whereas greater destruction of tubular cells than of glomeruli may lead to the so-called "tubular

diuresis." Likewise, a normal renal circulation is necessary for glomerulotubular balance.

It now seems clear that tubular reabsorptive activity is controlled, in part, by the activity of the endocrine system, the more important organs being the adrenal cortex and the pituitary gland. The role played by the former is best seen in the derangements that follow disease of the adrenal cortex. In Addison's disease it has been found that sodium loss is excessive because the renal tubules fail to reabsorb sodium owing to a deficit of cortical hormones, similar to, if not identical with, desoxycorticosterone acetate.³¹ In addition to sodium loss, potassium retention occurs. The fundamental change in the plasma concentrations of these two ions appears to account for many of the manifestations of the disease. Desoxycorticosterone in excess produces a syndrome of a contrasting character in which potassium is lost.³² Occasionally in Cushing's syndrome, a disorder in which hyperactivity of the adrenal cortex seems probable, hypopotassemia and sodium retention may occur.^{33, 34} There is no doubt that the pituitary gland elaborates substances having a powerful influence on renal tubular activity. The antidiuretic hormone is active in promoting the reabsorption of water and is necessary for normal water excretion. The absence or deficit of this agent has been shown to be responsible for the defect of water reabsorption in diabetes insipidus. This hormone, like the cortical hormone, has an influence on the tubular reabsorption of sodium and chloride.³⁵ Thus, there appears to be an excessive reabsorption of sodium in pituitarectomized animals that leads to edema formation when salt is added to the drinking water. The pituitary gland is also active in affecting other renal tubular functions, for it has been shown that the excretion of Diodrast and other substances is reduced following pituitarectomy³⁶ and enhanced by the administration of pituitary extracts.³⁷

Renal insufficiency may result in the loss or retention of water and salt, depending on the character of the renal lesion. Early in the course of renal disease, glomerulotubular imbalance may lead to increased reabsorption of water and salt, whereas later in the course, tubular diuresis results in loss. Since each of these substances is handled by more or less independent mechanisms, salt may be lost in excess of water or water in excess of salt, or the two may be retained independently in some degree.

Water and salt retention with the formation of edema occurs frequently in the course of many renal disorders, often in association with other evidence of renal failure. In the nephrotic syndrome, edema arises primarily from the renal loss of plasma protein with a resulting disturbance of the transcapillary balance of forces. In acute diffuse glomerulonephritis, edema apparently stems from the renal retention of water and electrolytes, although this

point is disputed by those who claim that congestive heart failure may be a factor³⁸ In this instance, a reduction of the glomerular filtration rate relative to the capacity of adjoined tubules is the cause of excessive reabsorption, as well as of azotemia It seems not unlikely that heart failure in such cases is the result rather than the cause of factors producing edema

Occasionally, renal failure results in retention of sodium and chloride, with loss of water³⁹ This situation, which is usually found when the structure of the kidney is not seriously disturbed by disease, probably implies an abnormality of water reabsorption in the distal segment The plasma and the extracellular fluid as a whole become demonstrably hypertonic Winkler and his co-workers⁴⁰ have shown, in a series of carefully planned experiments, that such a hypertonicity leads to the loss of water from the cellular compartment, probably accompanied by intracellular electrolyte This cellular dehydration at first is not serious, but it ultimately causes sudden death from respiratory failure^{40 41} Certain deaths in renal insufficiency in the absence of acidosis or cardiovascular abnormalities may occur on this basis

Recently, several interesting cases have been reported in which renal insufficiency, due to sulfonamide intoxication, was associated with severe injury to the brain and increased plasma concentrations of sodium and chloride Luetscher and Blackman³⁹ described 5 patients who developed oliguria and azotemia after the administration of varying amounts of sulfonamides In all, signs of central-nervous-system injury, such as confusion, delirium, stupor and coma, were observed Marked elevations of the serum chloride and sodium developed as the oliguria and azotemia receded, apparently because of excessive water loss in the urine without a corresponding loss of sodium and chloride It appears that the therapeutic administration of saline solutions had nothing to do with this phenomenon However, in 2 cases, death, as a result of pulmonary edema, followed the cautious intravenous administration of fluid At autopsy, areas of cerebral edema and gliosis were found, together with renal tubular lesions and thrombosis of the interlobular veins In 2 patients who survived the uremic stage, there was a slow and incomplete recovery from the effects of the central-nervous-system lesions

Symptomatology of this character may also follow overzealous administration of saline postoperatively⁴²⁻⁴⁴ Apparently, renal dysfunction, on the basis of incipient surgical shock, becomes more profound and uremia develops when the necessity for coping with large amounts of salt and water is superimposed Edema frequently develops Likewise, ill considered therapy may precipitate or intensify uremia when renal parenchymal damage is present.

In conditions such as diarrhea, pyloric obstruction and excessive sweating, dehydration may be associated with a loss of electrolyte in excess of water, especially when water is ingested without a supplement of salt Dilution of the plasma occurs, and water moves from the extracellular space into the cells When the loss of body water is sufficiently large, the plasma volume may be reduced Dehydration of this character occurs frequently during renal insufficiency The loss of the concentrating power and the failure of electrolyte-sparing processes lead to large losses of water and salt and usually result in acidosis

Recently, Thorn, Koepf and Clinton⁴⁵ described in detail 2 cases of so-called "salt-losing nephritis" The patients were admitted to the hospital in a state of shock, associated with azotemia and hyposthenuria A provisional diagnosis of Addison's disease in crisis was disproved in each case by a failure to improve after the administration of desoxycorticosterone acetate The administration of sodium chloride was followed by alleviation of the symptoms of collapse, but by no change in the signs of renal insufficiency Both patients ultimately died in uremia with hypertension In these patients, it appeared that the loss of sodium and chloride as a result of tubular damage, possibly associated with glomerulotubular imbalance, induced a rapid loss of water and a critical reduction of the plasma volume Such cases are rare Usually, there is a progressive dehydration The ingestion of water finally fails to correct this loss, and a state of lassitude, weakness, integumentary and mucosal drying and hyperpnea slowly develops

Hypochloremia is characteristic of these cases and is often observed during renal insufficiency⁴² Excessive salt loss, without serious depletion of the plasma volume, may produce a syndrome of muscle cramps, weakness, fatigability, apathy and mental confusion, as in heat cramps⁴⁶ Psychiatric disturbances in normal men suffering from protracted salt deficiency have been shown to respond to increases in salt intake⁴⁷ Thus, it is evident that routine restriction of salt when edema is not present may have serious consequences in uremic patients

Potassium

Potassium is the most important base held within the cells In this position it plays an essential role in the determination of intracellular osmotic pressure and water content Moreover, it apparently participates in some manner in the processes of intracellular metabolism⁴⁸

Reduction of potassium ion concentration in the fluid bathing muscle is known to cause decreased irritability It is possible that this factor is significant in the syndrome of familial periodic paralysis⁴⁹ This condition is characterized by periodic hypokalemia associated with losses of motor function, reflex activity and electrical excitability that im-

prove dramatically following potassium administration. This response appears to be specific, but its mechanism is not entirely clear, since hypokalemia of the same order does not usually cause paralysis, except in susceptible persons.⁴⁹ A similar state, however, has been produced in animals treated with desoxycorticosterone.⁵² Low serum potassium levels likewise cause abnormalities of cardiac muscular activity, giving rise to electrocardiographic changes consisting of depressed ST segments and low T waves.⁵⁰ Necrotic lesions of the myocardium have been induced in rats by overdosage with desoxycorticosterone and low-potassium diets.^{51, 52}

It is now evident that sufficiently high levels of potassium are also injurious to the heart.^{53, 54} In animals and men, anomalies of conduction occur when the potassium level exceeds 10 milliequiv per liter. These abnormalities result in increased height of the T waves, widened QRS complexes and evidence of progressive ventricular block. Death occurs in heart failure with cardiac arrest. No other manifestations of abnormal neuromuscular activity have been noted.

The study of potassium metabolism has suffered from the complexities inherent in the activity of this ion.⁴⁸ The relation between tissue and extracellular potassium, the balance between intake and renal excretion and the influence of the endocrine system are difficult to disentangle. Thus, the potassium clearance may change markedly from day to day in the same person and the plasma concentration may vary unpredictably, often without reference to potassium intake.⁵⁵ Since most of the potassium of the body is held within the cells, relatively small shifts of the ions into or out of the extracellular fluid might be expected to produce significant plasma concentration changes. On the whole, a dynamic balance appears to exist between the two major water compartments that permits active exchange of potassium.^{48, 56} Moreover, mass shifts may occur in response to alterations of water concentration or of tissue catabolism. These factors undoubtedly account for the apparently erratic behavior of plasma potassium.

✓It is possible, in view of recent evidence^{57, 58} that potassium is lost by the cells during acidosis. Apparently, the movement of potassium from the body during acidosis due to diarrhea in infants demands replacement therapy.⁵⁹ Recovery is more rapid and fatalities fewer under this regime. It is not unlikely that a similar situation arises during renal insufficiency when there is wastage of electrolytes. This may ultimately pose a problem of therapy in renal disease.

Ordinarily, the kidney does not permit excessive loss of potassium in the urine. The renal clearance is quite low, indicating extensive tubular reabsorption.⁴ When potassium is injected intravenously or given by mouth, however, the kidney excretes it rapidly. Although it is apparent that potassium is

handled independently of sodium by the kidney, some may be lost during a sodium diuresis. Satisfactory quantitative studies of potassium reabsorption have not been made.

Renal disease does not usually result in disturbances of potassium until it is far advanced.^{55, 60} Indeed, retention does not occur until anuria or extreme oliguria has developed.⁶⁵ This fact does not necessarily denote normal renal excretory function. Reduced tubular reabsorption may easily compensate for the reduction of filtered potassium and, indeed, seems evident in the demonstration by Keith and his co-workers⁵⁵ of potassium-inulin clearance ratios at or in excess of unity. These investigators suggest that the high ratios indicate tubular excretion, but in view of the questionable validity of the inulin clearance as a measure of filtration rate during renal insufficiency,⁶¹ this conclusion cannot be accepted. Although urinary loss of potassium might be anticipated, it has been observed less frequently than retention.

Potassium intoxication during uremia is as rare a therapeutic complication as it is a spontaneous development. Electrocardiographic changes and even fatalities due to cardiac arrest have been described following the use of potassium chloride for the purpose of inducing diuresis.^{62, 63} As a rule, dangerous retention does not occur, but the drug must always be given with caution when azotemia is present and never during anuria.⁶⁴ Spontaneous elevations of potassium, with sudden death, have been reported in chronic renal disease and in anuria.^{65, 66}

Recently Brown, Currens and Marchand⁶⁷ reported 3 cases with low potassium levels during chronic nephritis. In these patients episodes of apparent flaccid paralysis associated with electrocardiographic changes characteristic of hypokalemia were observed. Potassium chloride therapy was followed by symptomatic improvement and a return of the electrocardiogram to normal. Potassium-balance studies were not carried out. Although these findings resembled those of familial periodic paralysis, certain discrepancies were noted. On several occasions the episodes of motor disorder were characterized by stiffness and cramps that might have been caused by hypocalcemia or hypochloremia, which were present. Moreover, none of the patients presented the characteristic loss of tendon reflexes. In view of these divergencies and since it is difficult to induce the syndrome experimentally in human subjects, the conclusion that potassium depletion was responsible for the episodes of paralysis must be accepted with caution. Other cases of potassium depletion in which neuromuscular manifestations did not develop have been reported.^{68, 69}

Like sodium and water, potassium is subject to the influence of the endocrine system. The adrenal cortex is particularly active in this respect, produc-

ing an agent, like desoxycorticosterone, that stimulates the renal tubular reabsorption of potassium^{31, 32}. In the absence of the kidney this agent apparently has no effect on the plasma potassium concentration⁷⁰. It has been found, however, that potassium depletion⁷¹ or desoxycorticosterone may be effective in prolonging life during experimental renal insufficiency^{72, 73}.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

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CASE 32471

PRESENTATION OF CASE

A thirty-seven-year-old factory manager entered the hospital because of general malaise.

The patient was apparently well until four and a half months before entry, when he began to feel tired and "washed out." His job was trying at that time, and he returned home each evening with an extremely "tired," aching feeling in the legs. The aching became most marked when he sat with the legs hanging down, but there was no concomitant swelling of the ankles. Four months before entry, he developed a diffuse, crampy pain in the right upper quadrant of the abdomen. This was followed by tenderness in the same region and fever, the white-cell count was 18,000. The patient was taken to a hospital, where an inflamed appendix, located almost at the level of the umbilicus, was removed. He recovered rapidly and felt much better after the operation. Three and a half months before entry, several days after his return home, he was suddenly seized by a severe, sharp pain in the left back that was aggravated by breathing and was not relieved by strapping the back. He also developed increasing dyspnea, fever, prostration and a hacking, non-productive cough. After a week in bed with little improvement, he again entered the hospital. A chest x-ray film showed a large pleural effusion on the left, and 200 cc of pink fluid was removed. Six weeks before entry another chest film showed the diaphragm to be high on the left, there was considerable density in the left lower lobe and a small amount of fluid, with what seemed to be a pocket of air, in the left pleural cavity. For the next six weeks the patient had profuse sweats day and night. On one occasion he coughed up a small amount of blood. The chest pain gradually subsided under penicillin therapy. On discharge from the hospital, four weeks before entry, he was afebrile but he still had a mild cough, poor appetite, weakness and a sense of constriction in the left side of the chest. He resumed work on a part-time basis but was forced to stop because of marked fatigue. Three weeks later, x-ray films taken by a physician showed little change

from the findings on the previous examination except for slightly less pleural thickening.

The patient had always enjoyed good general health. He smoked about forty cigarettes a day and had five to seven drinks each evening. Since the onset of his illness he had lost about 30 pounds in weight.

Physical examination revealed a pale, sickly looking man in no distress. The left side of the chest, which was sunken in front, expanded only slightly on deep inspiration. Breath sounds were diminished over the base posteriorly. There were no moist or musical rales. There was tenderness in the right upper quadrant. The liver edge was somewhat tender and was palpated one and a half finger-breadths below the costal margin.

The temperature was 98.6° F, the pulse 96, and the respirations 20. The blood pressure was 135 systolic, 70 diastolic.

Examination of the blood showed a hemoglobin of 15.1 gm and a white-cell count of 9400 with 62 per cent neutrophils and 36 per cent lymphocytes. The urine was normal. X-ray examination of the chest showed a cavity containing air and fluid in the left side of the chest laterally, extending from the level of the fifth rib to the diaphragm. The cavity measured 3 cm in the anteroposterior view and 10 cm in the lateral view, with the fluid level at the eighth interspace. There was gross thickening of the axillary pleura, and the left diaphragm was elevated. The right lung field was clear, and the heart was not displaced. Bronchoscopy showed a good airway on the left, with no evidence of obstruction.

A needle inserted high in the right midaxilla went through thickened tissue and then into the air pocket seen on the x-ray film. The pressure with normal breathing was equivalent to +1 to -1 cm of water, but with deep inspiration it swung to -7 cm and with clearing of the throat it swung high enough on the positive side to force fluid out of the top of the manometer. After 60 cc of air had been removed from the cavity, 25 cc of thin, slightly cloudy fluid was withdrawn, toward the end the fluid was slightly pink. It contained 4600 red cells and 6400 white cells per cubic millimeter, all of which were polymorphonuclears. Chest x-ray films after the tap showed a slight decrease in the amount of fluid. On the fifteenth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. ALLEN BRAILEY. I do not know when I have read a more delightfully tangled web of clues and counterclues, real and spurious. This man's illness began with a tired, achy feeling in the legs. A month later he was suddenly seized with severe, sharp pain in the left back, — I assume that the term "left back" means the left lower chest in back. It would be easy to explain these particular symptoms as

having been due to thrombophlebitis of the lower legs, with subsequent pulmonary embolus. And he may have had both thrombophlebitis and embolism, but these events rarely occur in men under forty and the description of the chest pain does not sound much like embolism. It suggests pleurisy due to infection rather than infarction, for the record states that following the chest pain of sudden onset he developed increasing dyspnea, fever, prostration and cough. X-ray examination showed a large pleural effusion, and subsequent events suggested that the fluid removed from the pleura was infected and became an empyema. Effusion of more than a few cubic centimeters in association with pulmonary infarction is exceedingly rare, and empyema following an embolus from an early symptomless thrombophlebitis of the leg veins is, I think, unheard of. Consequently, if the patient had a pulmonary infarct of the usual leg-to-lung variety, I can only say that he had much else besides, and I do not know how to relate such an infarct to whatever else was present.

Let us drop the origin of the illness for the time being and consider the end result. Besides the effusion and empyema that were suspected, we are told that there was considerable density in the left lower lobe, that the left leaf of the diaphragm was high and that the left side of the chest seemed sunken in and showed little respiratory excursion. These observations can mean only that the lower lobe was largely collapsed owing either to increased pressure in the pleural space or to bronchial obstruction with absorption of the air behind the obstruction. The first x-ray examination revealed a large effusion, but the second plate demonstrated only a small amount of pleural fluid. Yet the lower lobe had not re-expanded, and the diaphragm had already risen to an abnormal position. The bubble of air seen in the left pleural space could easily have been drawn in on the occasion of the first thoracentesis. But it was not absorbed, it persisted, and in fact, the record suggests that it was distinctly larger when last observed than when first observed. Finally, there is the detailed information concerning the pressure found on the occasion of the last thoracentesis. It is possible, of course, for a pleural effusion to reach the precise volume to neutralize the negative pressure normally found in the pleural space, but it would be a most striking coincidence to have pressure readings taken at exactly the time when the intrapleural pressure was so neutralized. The fact that the pressures found on quiet breathing oscillated around zero ordinarily means only one thing: that the pleural space is in direct connection with the outside by way of a bronchopleural fistula. The fact that deep inspiration produced a negative pressure of 7 cm. of water suggests that the fistulous tract was small. But if there was a bronchopleural fistula, there was no bronchial obstruction. Therefore, why did the lobe collapse? First of all, collapse

does not require that the bronchus be completely obstructed. It simply requires that the cross section of the airway be reduced below a critical area. Furthermore, there is another possibility that we have not considered. Perhaps we are not dealing with normally elastic lung tissue. Perhaps this lower lobe or a good portion of it had been replaced by scar or by cancerous tissue. Cancer that had reached the pleura could and probably would have resulted in pleurisy with effusion, as well as in a fistulous tract between the pleura and a bronchus. What else can we find in favor of cancer? On the first chest tap, 200 cc of pink fluid was removed. Presumably it was bloodstained fluid. The blood may have resulted from the trauma of the tap. But the last tap is described as follows: "25 cc of thin, slightly cloudy fluid was withdrawn, toward the end the fluid was slightly pink." This account certainly suggests that the effusion contained a little blood that had settled into the lower portion of the cavity and that the blood was not the result of a traumatic tap. Also, after the early empyema had been successfully treated with penicillin, the patient did not do well, but in spite of being afebrile, he continued to have a mild cough, poor appetite and weakness, and he had to give up work because of marked fatigue. He is described as pale and sickly looking — symptoms and an appearance that are consistent with an advancing cancer of the bronchus.

What other diagnoses must be considered? Could the whole process in the chest have been due to tuberculosis? Perhaps it could. The location of the process and the speed with which it incapacitated the patient are unusual but not unheard of. If he had tuberculosis, however, the empyema was a tuberculous empyema, and even if due to mixed organisms it would not have responded so favorably to penicillin as this one apparently did. When the patient entered this hospital he was afebrile. Yet he was a very sick man and getting sicker. If the disease had been tuberculosis, he would certainly not have been afebrile at that stage. Finally, I am sure that appropriate laboratory tests were made to exclude tuberculosis, and since they are not even mentioned I am sure that they were negative.

Did the appendicitis have anything to do with the disease on admission? The patient may have had an abscess of the left lobe of the liver or a subphrenic abscess as a complication of the appendicitis, with subsequent rupture through the diaphragm to involve the pleura and the left lower lobe. The liver is described as somewhat enlarged and tender. This seems a rather fanciful hypothesis, and furthermore it is open to the same objection that during the hospital stay there was little evidence that infection was playing any major role. Yet the patient was not getting better.

Did he have a lung abscess of the ordinary gangrenous variety that ruptured into the pleural space? I should like to know how much sputum he raised,

whether it had any characteristic odor and what was the odor of the pleural fluid. Nothing is said of a fluid level inside the lung. Lung abscess is a poor guess. I think that the best I can do is to guess that at operation the left lower lobe was removed, or at least biopsied, and that cancer was found.

I do not know why I refused to see the x-ray films. Perhaps I should see them now.

DR JAMES R. LINGLEY: This first film, which was taken in the other hospital, shows the large pleural effusion on the left. This film was taken two months later and shows the air-containing cavity with a fluid level at the eighth rib. The first film taken here shows little change from the one taken a month previously. The cavity looks like a pleural rather than a pulmonary cavity. There is marked thickening of the axillary pleura, which suggests an empyema rather than an effusion. The lower lobe is not well visualized because of the change in the pleura, but it is probably partially collapsed. I think that the degree of collapse can be due to pressure from an empyema.

DR DONALD S. KING: I first saw this patient in my office. After he was admitted to the hospital, I discussed the case with the members of the refresher course and later with those of the Thoracic Clinic. The sequence of events seemed to point to the operation as the main etiologic factor. But the sequelae were unusual for a postoperative pulmonary infarct, and we all wondered whether some pre-existing condition accounted for the lung changes. I believe that most of the trouble before the operation was on an emotional basis. A man who smokes forty cigarettes a day and takes eight drinks of alcohol usually has something on his mind, and I know that this patient had plenty of things to worry him. Dates are important in consideration of this case. On May 29, the appendectomy was performed. He went home a few days after the operation. When he was at home, on about June 5, he developed a sudden pain in the left back and fever. On June 26 the x-ray film was taken that showed the large left pleural effusion. On June 27 the first chest tap was performed. On August 16 the x-ray film was taken that showed the pocket of air and fluid in the pleural cavity and the so-called "thickened pleura." On September 17 another chest x-ray film was taken that disclosed the persistence of the air pocket, his physician therefore reasoned that he must have a bronchial fistula and sent him to the hospital for study.

On physical examination we were impressed by the markedly diminished respiratory movement of the left side of the chest. The patient said that this loss of motion was becoming more and more noticeable. It seemed evident that unless something were done a permanent crippling would result. Consequently, after the chest taps, Dr. Churchill arranged to operate. I saw Dr. Churchill remove part of the lung and decorticate a considerable area. I

do not yet know what Dr. Mallory found when he examined the specimen. The only clinical explanation that I can give is that there was an aseptic pulmonary infarct, which was, as practically always, located close to the pleural surface, and that the area became necrotic and ruptured into the pleural cavity. There is no indication of the formation of a real putrid abscess in the area of an aseptic infarct. Cases are reported, however, in which such a condition is said to have developed. Do you believe that this can happen, Dr. Castleman?

DR BENJAMIN CASTLEMAN: Rarely.

DR KING: Recently, I read a paper that quoted you to that effect but went on to report a series of cases in which it was determined that true abscess had developed. But in this case there is no history of abscess.

DR LOUIS K. DAHL: I should like Dr. King to comment on Dr. Brailey's statement that pulmonary infarcts do not give pleural effusion. It is my impression that they frequently do.

DR BRAILEY: I do not believe that they cause empyema—that is, no more than a small amount of fluid. Dr. Homans was my authority.

DR KING: I am sure that large pleural effusions occur in association with pulmonary infarction. The cases that I remember particularly are those with post-delivery infarction, in which the fluid has been bloody. But I agree that, in a large series of pulmonary infarcts, the percentage in which a massive effusion occurs is small.

DR TRACY B. MALLORY: Dr. Churchill, will you tell us what you thought before operation and describe your operative findings?

DR EDWARD CHURCHILL: I do not wonder that Dr. Brailey found this a confusing case. Even after working in this man's chest for three hours I was still confused. Surgically, we were faced with two or three facts that led us to the treatment, irrespective of what we might call a rational basis for the interpretation of the disease. The patient had little respiratory excursion, owing to a frozen chest. He had been out of work and could not go back; he had tried conservative measures for about four months and finally concluded that he was making no progress.

I shall give you only the objective findings of the operation. In resecting the seventh rib I found the ribs close together and beginning to "shingle," as they do in chronic pleuritis. By a slow dissection of the thick parietal pleura, we were able gradually to spread the thoracotomy opening and expose the field. There was an air-filled cavity lined with pleura, about 1 cm thick. The cavity contained another 2 or 3 cc of the pinkish, cloudy fluid that Dr. King had removed. There was a membranous inflammatory partition within the cavity, which was easily opened. There was about 1 cm of rather thick, purulent material on the surface of the lung. That material was put into a test tube and sent over

for immediate smear and culture. The smear was negative, as had been both anaerobic and aerobic cultures from the fluid removed by Dr. King prior to the operation. We set ourselves the task of dissecting away the thickened pleura surrounding the cavity. This was extremely dense and slightly edematous and effectively bound down the lung. On the anterior surface of the lower lobe was an area where there was no thickened pleural membrane. Instead, there presented an area of the lung with thin visceral pleura and anthracotic markings. On making a slight incision the alveolar spaces were found to be filled with exudate. After cutting away the thickened pleural capsule, we were left with a "button" of lung surrounded by a fringe of thickened pleura. I therefore took a tangential slice off the lung to include the areas described. Cutting at a depth of about 1 cm. below it, the knife passed through normal aerated lung tissue with brisk pulmonary circulation and open bronchi. The process consequently did not extend deeply into the lung as one might expect had it been hemorrhagic infarction. I hope that we cured the man. When he left the hospital, the chest was moving freely and he felt better. We straightened out the lower lobe, liberated the diaphragm and restored the chest to as nearly normal as possible. We shall await Dr. Mallory's report before trying to interpret the disease.

CLINICAL DIAGNOSIS

Empyema, left chest

DR. BRAILEY'S DIAGNOSIS

Bronchiogenic carcinoma

ANATOMICAL DIAGNOSES

Infarction of lung (? septic).

Fibrous pleuritis

Chronic pneumonitis

Bronchiolectasis

PATHOLOGICAL DISCUSSION

DR. MALLORY. I am not sure that I am going to help much in the interpretation, as so often happens in cases that are rather obscure clinically. I shall try to show what Dr. Churchill found. A piece of white tissue represented what was left of the greatly thickened pleura. In the center was a mass—the "button"—projecting through the gap in the dense fibrous tissue—that had the appearance of lung tissue. Microscopic sections from this area showed that the thickened pleura was merely dense granulation tissue of the type that one sees in the wall of an empyema cavity or an organized hematoma. The nubbin of herniating lung tissue was completely necrotic and looked rather like infarction, although its character was different from the ordinary infarction. The average infarct of the lung is deeply hemorrhagic and firm. This tissue was soft, and

blood pigment, if it was present, had been largely absorbed.

The specimen that Dr. Churchill gave us also included a certain amount of underlying lung tissue that showed a complicated picture. There was an extensive chronic pneumonitis, as well as some large dilated bronchioles surrounded by marked inflammatory infiltration. This was a superficial specimen, and I think that the presence of such large bronchioles must be considered as indicating bronchiectasis. There was also an area in the deeper lung tissue that showed dense scarring, with concentration of elastic fibers, which is characteristic of healed infarction. Finally, there were a number of blood vessels containing organized thrombi. I am certain that there was infarction in this case. I am tempted to believe that there was some preceding pneumonitis of much older duration than the history indicated, although I am not entirely certain about that. Why the wall of the empyema cavity contained a gap and the lung herniated through that gap, I cannot guess, unless the wall had been lacerated in one of the preceding taps. The wall was so thick, however, that I find it difficult to believe that a needle could have produced a laceration 2 cm. long.

Have you any further comments, Dr. Churchill?

DR. CHURCHILL. There is one variable here that I think we must remember, although I cannot be certain of its significance. If we start at the beginning with an ordinary post-infection empyema, such as may occur after a superficial carbuncle, a mastoiditis or an appendicitis, we know that the empyema would probably develop a bronchial fistula because it has originated from a small abscess beneath the visceral pleura. If the empyema in the case under discussion had been recognized at that time, if a streptococcus had been cultured and if a surgeon had drained it, I think that our findings would have been accepted without any confusion. Actually, what did happen? The illness was treated with penicillin, and we have no record of a positive culture. I cannot picture this type and degree of chronic pleuritis originating other than by invasive infection. I state it as a series of questions. Was there a small metastatic abscess—possibly an infarct, because it was borne by the blood stream but not in the sense of a hemorrhagic infarct associated with thrombophlebitis—beneath the visceral pleura that caused the empyema? Was the invasive infection brought under complete control by chemotherapy? Did the rupture of this abscess produce the chronic pyopneumothorax and the chronic pleuritis? Having had difficulty in cutting the pleura with a knife or scissors, I cannot see how it could have been lacerated by an aspirating needle, but what the mechanism was that left the exposed area of lung, I do not know.

DR. KING. You would not have drained early would you? It was very thin fluid—never gross pus.

DR CHURCHILL I do not know

DR KING That fluid could probably have been taken out with a needle

DR CHURCHILL Perhaps if it had been removed with a needle and penicillin had been administered, the result would have been different

Was the patient tapped on the sixth day following operation?

DR KING Two or three weeks afterward The first chest tap was made four weeks after operation

CASE 32472

PRESENTATION OF CASE

A seventy-six-year-old physician entered the hospital because of painless jaundice

Three months before admission, prostration, nausea and vague abdominal pains without diarrhea occurred twelve hours after the patient had eaten a cold salad at a public gathering. He spent two weeks in another hospital, where a barium enema was interpreted as showing ulcerative colitis. One stool examination gave a ++++ guaiac reaction, but a subsequent one was negative. An upper gastrointestinal series revealed a normal appearing esophagus, stomach and small intestine. A single large gallstone was visualized. After this episode the patient never regained his appetite. He lost weight and felt increasingly tired and ill. A diffuse vague abdominal discomfort persisted. There was no change in bowel habits and no chills or fever. Three weeks before admission painless jaundice developed insidiously, and anorexia became more pronounced, the stools became clay colored, and the urine became dark. The patient had been losing weight and feeling tired for six or seven months.

Three years before admission the patient had been admitted to a hospital after an acute episode of vertigo with nystagmus. There were no headaches. For many years he had been accustomed to drinking Scotch whisky and soda at bedtime and three or four highballs during the week.

On physical examination the scleras and the skin were yellow. The heart and lungs were normal. The liver edge was palpated 6 cm below the right costal margin and 12 cm below the xiphoid. The upper border was percussed in the fifth interspace. The left lobe was harder and tenderer than the right. The hepatic surface felt smooth. The abdomen was slightly distended, but there were no signs of fluid. The spleen was not palpable. The prostate was twice the normal size. There were external hemorrhoids.

The temperature was 98.0° F, the pulse 60, and the respirations 20. The blood pressure was 124 systolic, 70 diastolic.

Examination of the blood showed a hemoglobin of 13.6 gm per 100 cc and a white-cell count of 13,000, with 78 per cent neutrophils. The urine

gave a + test for albumin and a ++ test for bile, the sediment contained rare hyaline casts, rare red cells and occasional white cells per high-power field. X-ray films of the gastrointestinal tract showed evidence of an extrinsic mass compressing the lesser curve of the stomach in the region of the left lobe of the liver. The duodenal cap likewise showed evidence of an extrinsic pressure along the lesser curvature margin. There was a suggestion of small esophageal varices. A laminated, round opacity was seen in the region of the gall bladder. The liver was considerably enlarged and the spleen slightly so. The previous films were reviewed by another observer, who failed to find evidence of ulcerative colitis. The serum cholesterol was 188 mg, the non-protein nitrogen 35 mg and the total protein 5.8 gm per 100 cc with 3.5 gm of albumin and 2.3 gm of globulin. The alkaline phosphatase level was 19.3 Bodansky units per 100 cc. The cephaloflocculation test was + in twenty-four hours and ++ in forty-eight hours. The prothrombin time was 22 seconds (normal, 18 seconds). The stools were neutral yellow and gave a negative reaction for blood.

Two days after admission the patient was obviously losing ground. The jaundice became a deep-orange color, and the abdomen became moderately distended. On the fourth hospital day a fluid wave was elicited. On the sixth day, the stools became definitely brown and contained bile. On two occasions the patient vomited small amounts of fluid containing gross blood. There was no sign of massive hemorrhage. On the seventh day the patient was more comfortable and seemed to be stronger. On the eighth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR EARLE M. CHAPMAN We are presented with a seventy-six-year-old physician who had been losing weight and feeling tired for six or seven months. He had the first acute episode three months before entry and developed painless jaundice two months later. On physical examination, there was a palpable mass, apparently somewhere in the epigastrium. It is stated that the left lobe of the liver was harder and tenderer than the right, and on x-ray study this mass appeared to be extrinsic, compressing the lesser curvature of the stomach and duodenum. A single diagnosis seems to be difficult indeed, and I think that we must go through a number of possibilities, any one of which I can name with no assurance.

At this age the story of weight loss, the illness of six months and the mass make one suspect the presence of tumor. What kind of tumor was it? I do not believe that it was carcinoma of the head of the pancreas causing painless jaundice. From all these findings I doubt that it was a lymphoblastoma in the retroperitoneal area that caused pressure on the

biliary system and an obstructive type of jaundice. Was it a primary liver tumor — possibly a hepatoma — that involved the left lobe of the liver? From the description I think that that is a possibility to be seriously entertained.

We must also consider an infectious process. Did the surgeon cure this man at operation? I am curious to know the preoperative diagnosis, because if the surgeon cured him, it is an amazing case. The evidence for infection is not great, but we must certainly think of it, especially when we are told that three months before admission there was a sudden episode of abdominal pain and blood in the stool on one occasion and that ulcerative colitis was suspected. But examination in this hospital did not disclose blood in the stool.

Did the patient have a large amebic abscess involving the left lobe and causing necrosis of liver tissue in that region, with jaundice, and pressure on at least a branch of the biliary system, with signs of obstructive jaundice? We learn that later in the hospital stay the stools changed in appearance and contained bile, so that there must have been a channel through which bile passed.

We know that this man had a gallstone. It is therefore possible that he had other gallstones, one of which formed higher in the biliary tree and lodged in the tributary of the common duct from the left lobe of the liver, thus causing obstructive phenomena in the left lobe.

The important decision to make is whether or not the patient had cirrhosis. I am going to say that it is unlikely in this case, because the signs were those of acute liver injury — the prothrombin time was normal, the spleen was not felt by the examiner and the total protein was normal. If this had been cirrhosis of any duration I am sure that the total protein would have been lowered, since it is usually an important indication of cirrhosis. Possibly, this was a subcirrhotic phase of liver disease. The patient drank Scotch whisky during the last few years, but he was not a wine drinker.

The other conditions that I think of are extremely unlikely. I might name a host of rare diseases, but I do not see how they could be entertained. In conclusion I should like to say that I believe that the patient had a primary tumor of the liver, probably a hepatoma of the left lobe, and that if he had cirrhosis it was of minimal degree and was not a portal cirrhosis of severe extent, I do not really believe that cirrhosis was present, however. My next choice is infection with amebic abscess, and finally the possibility of a stone lodged in a tributary from the left lobe of the liver and causing necrosis of tissue beyond that in an isolated lobe of the liver. One of these things, in the order given, is what I believe was found at operation.

DR. DANIEL ELLIS. If the patient had had a hepatoma, would there not have been more evidence of cirrhosis?

DR. CHAPMAN. It is true that a hepatoma is usually associated with cirrhosis, but it is possible without cirrhosis. I think that the normal protein indicates that the remainder of the liver was normal or almost so.

DR. JAMES TOWNSEND. If the patient had a tumor that completely obstructed bile through the intestine at the time he came in, how do you account for the reappearance of the bile?

DR. CHAPMAN. On a mechanical basis I think that when the patient was staggering around and upright there was pressure on the common duct, but that when he was lying down the pressure subsided and the bile went through.

DR. LAURENCE ROBBINS. What about the presence of varices in the absence of cirrhosis?

DR. CHAPMAN. I really do not know. The record states that there was a suggestion of varices, but that was merely a guess. I do not believe that we can rely on that statement in the face of the other findings.

DR. ROBBINS. I examined the patient and suspected that the tortuosities of the folds of the lower esophagus were varices.

DR. CHAPMAN. That is a matter of interpretation. We often see a suggestion of varices.

DR. ROBBINS. The mass and the defect in the lesser curvature of the duodenal cap were constant during the examination. The gallstone was previously described. The spleen was not large, it was slightly above the limits of normal. It was not typical of the spleens that are usually seen in cirrhosis, but I do think that varices were present.

DR. CHAPMAN. Then, of course, we have the fact that the patient drank Scotch whisky, which I regret to say is again in favor of cirrhosis.

A PHYSICIAN. What about the prostate in relation to tumor?

DR. CHAPMAN. The prostate was enlarged to twice the normal size. From the description, I assumed that it was soft and not irregular. I think that metastases from a prostate of this size are extremely unlikely.

DR. ELLIS. Our reasoning was much like that of Dr. Chapman. We thought that this man had obstructive jaundice and that the diagnosis was most probably cancer. With that in mind we advised him to enter the hospital for exploration. He came in three weeks later. Several striking things were noted in the eight days in the hospital. One was the steady decline in his condition. Although he had absolutely no fluid at the time of admission, in three days he had so much fluid in the abdomen that the abdominal viscera could no longer be palpated. This sudden reaccumulation of fluid was difficult to explain. The physical examination as described may be misleading, but there was no question in the minds of the men who felt the abdomen that the mass was the left lobe of the liver as nearly as one could palpate through the abdominal wall.

As Dr Chapman has pointed out, we thought that the blood chemical findings afforded little basis for a diagnosis of extensive intrinsic liver disease. Again, it seemed that this patient had cancer, and he was explored. The impression about the stools is correct: he had clay-colored stools three weeks before admission and for two days after admission, after which they became brown. At operation the surgeon made an incision about 15 cm long and was able to palpate the liver. The left lobe immediately came into view, and the entire liver had a finely granular surface and was yellowish brown and firmer than normal. The surgeon did not find any mass elsewhere in the abdomen. The gall bladder was not palpated. A fairly large section was taken from the right lobe of the liver for biopsy. The cut surface looked yellow and necrotic in places, and in the biliary tree there was a white, friable substance that was unlike anything we had ever seen. We thought that it was a severe necrotizing process in the liver. We did not believe that it was cancer. Because of the patient's poor condition it was decided that the primary condition was severe generalized intrahepatic disease—that was causing all the symptoms and that he should not have further exploration but should be treated from that standpoint. Therefore, no other exploration was done, and the abdomen was closed. The patient steadily failed and died two days after operation.

CLINICAL DIAGNOSIS

Carcinoma of liver, primary

DR. CHAPMAN'S DIAGNOSES

Hepatoma
Cirrhosis?

ANATOMICAL DIAGNOSES

Hepatoma
Cirrhosis of liver, alcoholic type
Tumor thrombi, portal vein and left hepatic duct.
Ruptured esophageal varix, with hemorrhage into gastrointestinal tract.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The biopsy showed an alcoholic type of cirrhosis as well as a hepatoma. The tumor tissue, which was for the most part necrotic, could be seen in some of the venous channels. At autopsy a few days after operation, the stomach and intestines were full of blood. Apparently, there had been a rupture of an esophageal varix. The spleen weighed 210 gm. The liver at autopsy weighed over 2000 gm, and the right lobe contained diffusely cirrhotic nodules, averaging 2 to 3 mm in diameter, and showed little tumor. The medial aspect of the right lobe, as well as the entire left lobe, was infiltrated with tumor. The portal vein and its radicles within the liver were filled with tumor, which is quite frequent in primary carcinoma of the liver. An interesting finding was the presence of tumor within the left intrahepatic duct. Apparently the tumor had extended through the liver tissue into the bile duct and had produced partial occlusion; it is possible that it had something to do with the change in the color of the stools. There was a stone in the gall bladder but no evidence of stone within the common duct.

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BIGELOW'S ORIGINAL ANNOUNCEMENT

On November 18, 1846, the *Boston Medical and Surgical Journal* had the privilege of publishing the first detailed public announcement to the medical profession of Morton's demonstration of surgical anesthesia at the Massachusetts General Hospital on October 16 of the same year. The paper was written by Henry Jacob Bigelow, a Boston surgeon of twenty-eight, who had witnessed the first operation and the second, on October 17, and had forced the issue to disclose the nature of the new agent at the time of a third operation on November 9. In the meantime Bigelow made a brief statement on the subject at a meeting of the American Academy

of Arts and Sciences on November 3. Moreover, the published paper was presumably essentially the same paper as that communicated by Bigelow to the members of the Boston Society of Medical Improvement on November 9, the day on which the third demonstration at the Massachusetts General Hospital took place. This operation, a formidable amputation, must have fully convinced young Bigelow of the simplicity and safety of ether insensibility, even if he was in any way doubtful of its value prior to November 9.

Bigelow's paper is probably the most important medical announcement ever to be so issued and thus brought to the attention of the medical profession, as is pointed out in a paper published elsewhere in this issue of the *Journal*. Although news of the first demonstration had been published in both the *Boston Daily Journal* and the *Daily Evening Transcript* on the next day, October 17, and Bigelow had talked about this and subsequent operations to local societies, the news did not have the ring of complete authenticity until it was printed in a well recognized, although small, accredited medical journal. The standing of the surgeon, John Collins Warren, was of international renown. So was the reputation of young Bigelow's father, Jacob. If the latter's oldest son, Henry Jacob, was not so well known outside Boston, at least his name was accepted, and the clear account, skillfully worded, was a document of prime importance, which was readily snatched up by eager hands in both America and abroad. Morton was indeed fortunate in his official announcer for in a few months "anesthesia," a name given to the state of insensibility produced by ether by Oliver Wendell Holmes in a letter to Morton dated November 21, 1846, became a world-wide procedure. That the first practical application of the method was an epoch-making event was fully recognized by the editor of the *Journal*, Dr. J. V. C. Smith, for there appeared in the same number as Bigelow's paper the following editorial calling attention to the article and its significance.

Operations without Pain.—In the leading article of this day's *Journal*, by Dr. H. J. Bigelow, the profession will notice that an impression exists here in Boston that a remarkable discovery has been made. Unlike the farce and tragedy of mesmerism, this is based on scientific principles, and is held in the names of gentlemen of high professional attainments, who make no secret of the matter.

or manner To prevent it from being abused and falling into the power of low, evil-minded, irresponsible persons, we are informed that the discoverer has secured a patent, and that means were taken to have the same security in Europe even before publicity was given to it here Without further remarks, we cheerfully publish all that has been given us on the subject, and wait with impatience for the decision of the profession in regard to its real value

Bigelow's communication was reprinted the next day in the *Boston Daily Advertiser*, Bigelow had the paper reprinted himself, and the *Hartford Courant* printed it as a supplement to the issue of December 26, 1846 The reprint in the *Advertiser* was sent, with a letter, by Jacob Bigelow to Francis Boott, of London, who arranged for publication in the *Lancet* on January 2, 1847 Robert Liston, aware of Jacob Bigelow's letter, operated on December 21, 1846, "with the most perfect and satisfactory results" The "new gas" had been accepted by competent surgeons, both in this country and abroad, in a few months, so that the editor's "impatience" was not of long duration Medicine's greatest single gift to suffering humanity thus was distributed rapidly and efficiently, even taking into account the rate of communication in vogue in 1846 Bigelow's paper was the announcement that gave authenticity and substance to the gift

PROVERBS 23:20

NEVER, it is safe to assume, have so many people been so conscious of their dietary habits and the difficulty of obtaining various articles of food as during the present year Among the ancient and crowded populations of the earth this difficulty has produced mass hunger and, in places, nearly mass starvation, it is the worst of the famines that have periodically visited these unfortunate peoples In other countries, such as our own, where real want has scarcely been known since the early colonists were reduced to their few kernels of corn, an artificial

scarcity of certain items, resulting almost entirely from the recent attempts at price control, has been succeeded by an uncontrolled price inflation that may send these same articles beyond the reach of many people

During the war, when much of the meat supply was rationed, every excuse was made and practically every disease was used as an excuse to obtain extra rations Subsequently, when meat was still difficult

to obtain, whether because of scarcity or because of high prices, there were no committees to intervene on behalf of the patient with liver damage, with suppurative disease or with other wasting illness As of the fall of 1945, when all foods except sugar were removed from the ration list, it was every man for himself and the devil take the hindmost.

Fortunately the present situation is not so

bad as it seems, for we can now refer to a lesson that was taught us during the war years if we cannot afford meat, we can still get along without it Our protein requirements can be met by a variety of foods besides red meat, and iron in almost any form is the substance best adapted to the prevention and cure of the simple anemias

Red meat is not a necessity in any man's diet it is, in fact, possible to get along tolerably well and to endure at least a reasonable span of years without meat of any color George Bernard Shaw, whose somewhat choleric point of view can certainly not be attributed to overindulgence in the roast beef of Merrie England, has, among others, demonstrated this *Homo sapiens* can, in fact, according to recent observations, do quite well on as little as 50 grams of protein per day, in place of the traditional 70 grams, and of this as little as 5 grams need be in the form of animal protein But this is probably hewing too close to the line for Occidental alimentation, in the East, vast populations have sub-

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund For further information apply to

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

ted fairly well for centuries, — barring seasons
famine, — and there, even in time of plenty, less
an 10 per cent of the total protein intake is from
animal sources

Appetite and availability of food have largely
etermined our own eating habits, and the eating
abits of a people cannot be taken lightly, the most
ecetic of us enjoys a certain sense of well being
hen sitting before a roast of prime beef or a medium
urion steak We need not pretend, however, that
is a necessity so far as physical health is concerned
or that purpose a serving of finnan haddie or a few
tablespoonfuls of soy beans will do as well

Even if the desperation of our days forces us to
be among the winebibbers, circumstances have at
least spared us from being among the notorious eaters
of flesh

MISCELLANY

NOTES

The following appointments to the teaching staff of Har-
vard Medical School were recently announced Harold
Samuel Albert, of Boston (A B McGill University 1942,
M.D. McGill University 1943), assistant in psychiatry,
Richard William Anderson, of Boston (S B University of
Minnesota 1941, M.D. University of Minnesota 1943),
assistant in psychiatry, Robert Eugene Arnot, of Boston
(A.B. University of Minnesota 1937, M.D. Harvard Uni-
versity 1940), research fellow in psychiatry, Lionel Berk-
er, of Cape Town, South Africa (B S. University of Cape Town
1936, Ph.D. University of Cape Town 1939, M.B., Ch.B.
University of Cape Town 1939, M.D. University of Cape
Town 1944), research fellow in medicine, Bernard Bloom,
of Dorchester (A B New York University 1935, M.D. New
York University 1938), assistant in genitourinary surgery,
Wladislaw Joseph Borkowski, of Wilmington, Delaware (B S.
Villanova College 1939, M.D. Jefferson Medical College
1943), assistant in psychiatry, Thomas Berry Brazelton, of
Waco, Texas (A B Princeton University 1940, M.D. Colum-
bia University 1943), assistant in pediatrics, Harold Brown,
of Boston (A B Harvard University 1940, M.D. Harvard
University 1943), assistant in medicine, Henry Bunting, of
Wellesley (A B Yale University 1932, A.M. University of
Wisconsin 1934, M.D. Harvard University 1936), research
fellow in anatomy, Walter Edmund Campbell, of Provid-
ence, Rhode Island (S B Providence College 1937, M.D.
Jefferson Medical College 1941), assistant in psychiatry,
Russell LeGrand Carpenter, of Medford (S B Tufts College
1924, Ph.D. Harvard University 1928), instructor in ophthal-
mology, Donald Tillinghast Chamberlin, of Brookline (A B
Washington University 1926, M.D. Washington University
1930), assistant in medicine, William Rozelle Christensen,
of Salt Lake City, Utah (A B University of Utah 1938,
M.D. Harvard University 1942), research fellow in biological
chemistry, Theodore Sabin Cobbe, Jr., of Canton, Ohio
(A B Kenyon College 1940, M.D. Harvard University
1943), research associate in comparative pathology and
tropical medicine, William Hamilton Daughaday, of Fram-
ingham (A B Harvard University 1940, M.D. Harvard
University 1943), research fellow in medicine, Patrick
Macarney de Burgh, of Bymble, New South Wales (M.B.,
B.S. University of Sydney 1939), research fellow in bac-
teriology and immunology, Briant LeRoy Decker, of Brook-
line (A B Brigham Young University 1924, M.D. Harvard
University 1930), assistant in medicine, William Anderson
Decker, of Jamaica Plain (A B Harvard University 1936,

M.D. Cornell University 1943), assistant in pediatrics,
Frank James Dixon, Jr., of St. Paul, Minnesota (S B Uni-
versity of Minnesota 1941, M.B. University of Minnesota
1943, M.D. University of Minnesota 1943), research fellow
in pathology, Brown Melvaine Dobyns, of Cambridge
(A B Illinois College, 1935, M.D. Johns Hopkins Univer-
sity 1939, M.S. [in surgery] University of Minnesota 1944),
research fellow in surgery, Vincent Paul Dole, Jr., of Brook-
line (A B Stanford University 1934, M.D. Harvard Uni-
versity 1939), research fellow in medicine, Jack McCallum
Evans, of Buffalo, New York (A B Denison University
1935, M.D. University of Buffalo 1939), research fellow in
medicine, Russell Sylvester Fisher, of Alexandria, Virginia
(S B Georgia School of Technology 1937, M.D. Medical
College of Virginia 1942), research fellow in legal medicine,
Joseph Michael Foley, of Dorchester (A B Holy Cross
College 1937, M.D. Harvard University 1941), assistant
in neurology, Dan Hertz Funkenstein, of Jacksonville,
Florida (S B University of Georgia 1930, M.D. Tulane
University 1934), assistant in psychiatry, Watkins Proctor
Harvey, of Lynchburg, Virginia (A B Lynchburg College
1939, M.D. Duke University 1943), research fellow in medi-
cine, Paul Henry Harwood, Jr., of Chestnut Hill (A B
Princeton University 1935, M.D. Harvard University 1939),
assistant in psychiatry, Lester Lee Hasenbush, of Boston
(S B University of Chicago 1934, M.D. Johns Hopkins
University 1938), instructor in psychiatry, Marjone Hayes,
of Princeton, New Jersey (A B Vassar College 1937, M.D.
Johns Hopkins University 1942), assistant in psychiatry,
N. Paul Isbell, of Denver, Colorado (A B University of
Denver 1926, M.D. University of Colorado 1930), research
fellow in pathology, Herbert Jaffe of Brookline (S B Mas-
sachusetts Institute of Technology 1939, Ph.D. Massachu-
setts Institute of Technology 1943), research fellow in
medicine, Nathaniel Kengsberg, of New Haven, Connec-
ticut (A B Wesleyan University 1934, M.A. Wesleyan
University 1935, M.D. Yale University 1939), assistant in
surgery, John Albert Kneipp, of Washington, D.C. (A B
Duke University 1937, M.D. Duke University 1943), re-
search fellow in psychiatry, John Junior Kneisel, of Pelham
Manor, New York (M.D. Harvard University 1938), as-
sistant in surgery, Bernard Koechlin, of Basel, Switzerland
(Sc.D. University of Basel 1943), research fellow in physical
chemistry, Israel Kopp, of Dorchester (M.D. Tufts College
1927), research fellow in psychiatry, Francis Robert Lane,
of Somerville, Massachusetts (A B Harvard University
1940, M.D. Harvard University 1943), assistant in ob-
stetrics, Angelo Lapi, of Forty Fort, Pennsylvania (M.D.
University of Buffalo 1937) research fellow in legal medicine,
Henri Louis Marie Le Brignand, of Paris, France (B S. Uni-
versity of Paris 1931, M.D. Paris Medical School 1941),
research fellow in surgery, Julius Levine, of Dorchester
(M.D. Tufts College 1929), assistant in psychiatry, Mao-
chih Li, of Peiping, China (M.B. Medical School of Peiping
University 1929) research fellow in physiology, Rene Albert
Stephan Maurice Lontie, of Louvain, Belgium (D.Sc. Chim.
University of Louvain 1942), research fellow in physical
chemistry, Robert Alvan MacCready, of Melrose (S B
Dartmouth College 1925, M.D. Harvard University 1932),
instructor in bacteriology and immunology, Charles Alexan-
der MacGregor of Rumford, Maine (A B Colby College
1938, M.D. Harvard University 1942), assistant in sur-
gery, Nicholas Henry Martin, of Newcastle upon Tyne, Eng-
land (B S. Durham 1928, B.A. Oxford University 1933,
M.A., B.M., B.Ch. Oxford University 1937, M.R.C.P. Lon-
don University 1939), research fellow in pediatrics, Henry
Harcourt Waters Miles, of New Orleans Louisiana (S B
Tulane University 1936, M.D. Tulane University 1939),
research fellow in psychiatry, John Pervis Milnor, Jr.,
of Memphis, Tennessee (S B Yale University 1940, M.D.
University of Tennessee, College of Medicine 1942), re-
search fellow in medicine, Naum Mittelman, of Buenos
Aires, Argentina (Ph.D. Buenos Aires University 1942)
research fellow in physical chemistry, Herbert Roy Morgan,
of Riverside, California (A B University of California
1936, A.M. University of California 1933, M.D. Harvard
University 1942), research fellow in medicine, Thomas
Lynch Murphy, of Salisbury, North Carolina (A B Uni-
versity of North Carolina 1940, M.D. Harvard Univer-
sity 1943), research fellow in medicine, Roderick Murray,
of Wollaston (B S. University of Witwatersrand 1930, M.Sc.
University of South Africa 1931, M.D. Harvard Univer-

sity 1941), research fellow in medicine, Bo Norberg, of Stockholm, Sweden (M D Karolinska Institutet, Stockholm, 1942) research fellow in physical chemistry, Herbert William Park, III, of Greensboro, North Carolina (S B University of North Carolina 1944, M D Duke University 1945), research fellow in physiology, Walter Pick, of Wingham, Connecticut (M D Harvard University 1942), research fellow in pediatrics, Hele Sinclair Pittman, of Cambridge (A B Smith College 1921, M D Johns Hopkins University 1927), instructor in medicine, Sam Madison Powell, of Waco, Texas (S B University of the South 1934, M D Tulane University 1938), assistant in pediatrics, Charles Edward Rath, Jr., of Cleveland, Ohio (A B College of Wooster, 1940, M D Western Reserve University School of Medicine 1943), research fellow in medicine, Charles Washington Robertson, of Boston (A B Syracuse University 1935, M D Syracuse University 1939), assistant in surgery, Robert Rustigan, of Medford (S B Massachusetts State College 1938, S B Brown University 1940, Ph D Brown University 1943), research fellow in bacteriology and immunology, Harold Scheraga, of Brooklyn, New York (S B College of the City of New York 1941, A M Duke University 1942, Ph D Duke University 1946), research fellow in physical chemistry, Arnold Segel, of Cambridge (A B Harvard University 1932, M D Harvard University 1936), assistant in surgery, Nils Bengt Skanse, of Upsala, Sweden (M D University of Upsala 1945) research fellow in medicine, Lloyd Hollingsworth Smith, Jr., of Easley, South Carolina (A B Washington and Lee University 1944, medical student at Harvard from January 1944 to present) research fellow in physiology, Armando Soto-Rivera, of Caracas, Venezuela, South America (D M University Central de Venezuela 1943), research fellow in physiology, Herbert Carl Stoerk, of New York, New York (M D University of Vienna 1938) instructor in bacteriology and immunology, Melvin Irving Sturnick, of Allston (A B Harvard University 1935, M D Tufts College 1939), assistant in medicine, Yale Jerome Topper, of Cambridge (S B Northwestern University 1942, A M Harvard University 1943, Ph D Harvard University 1946), research fellow in biological chemistry, George Loughlin Tully, Jr., of West Newton (A B Boston College, 1941, M D Tufts College 1944), assistant in obstetrics, John Wily Garrett Tuthill, of Evanston, Illinois (A B Princeton University 1940, M D Harvard University 1943), research fellow in medicine, Bert Lester Vallee, of Brookline, Massachusetts (M D New York University 1943), research fellow in medicine, William Rhoads Waddell, of Tucson, Arizona (S B University of Arizona 1940, M D Harvard University 1943), research fellow in legal medicine, Roscoe Legrand Wall Jr., of Winston-Salem, North Carolina (S B Wake Forest 1936, S B in medicine Wake Forest 1938, M D Jefferson Medical College 1940), assistant in obstetrics, Hans Heugh Wandall, of Copenhagen, Denmark (A B Oestere Borgerdydskole, Copenhagen, 1933, M D University of Copenhagen 1940), research fellow in surgery, George Wingate Waring, Jr., of Columbia, South Carolina (S B University of South Carolina 1940, M D Johns Hopkins University 1943), assistant in pediatrics, Stanford Wessler of Albany, New York (A B Harvard University 1938 M D New York University 1942), research fellow in medicine, LeMoyne White of Walpole, New Hampshire (A B Harvard University 1936, M D Harvard University 1940), assistant in psychiatry, Joan Hilma Whittaker, of Peterborough Ontario (B S McGill University 1938) research fellow in obstetrics, James Paul Whittemore, of Somerville Massachusetts (A B Holy Cross College 1942, M D Harvard University 1945), assistant in pediatrics, and Norman Zamcheck, of Swampscott (A B Harvard University 1939, M D Harvard University 1943), research fellow in legal medicine

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Haverhill, Massachusetts

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(Notices on page vii)

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The New England Journal of Medicine

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Number 22

SYMPOSIUM ON GASTROINTESTINAL BLEEDING*

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS OF GASTROINTESTINAL BLEEDING

CHESTER M. JONES, M.D.†

BOSTON

ANY consideration of bleeding from the gastrointestinal tract holds the immediate implication that the problem may be either medical or surgical. This is of primary importance and must never be forgotten, either in the discussion of the general problem or in the making of decisions in the individual case. Because of the possible necessity of surgical intervention, gastrointestinal hemorrhage must invariably be considered from three distinct points of view. It must be thought of in terms of the actual site of the bleeding, which implies the necessity for accurate diagnosis whenever possible. The mechanism underlying the hemorrhage must also be carefully evaluated so that proper therapeutic measures may be decided on. The third consideration is the condition of the patient who is bleeding. Even before diagnostic or definitive therapeutic measures are undertaken, a decision must be made regarding the urgency of the situation in terms of shock and circulatory collapse.

A clear differentiation is needed between abrupt hemorrhage of shock proportions and minor oozing that, in the long run, may lead to more or less serious grades of anemia but is not an immediate threat to life. In major acute episodes the immediate concern is the safety of the patient. Even under the pressure of exsanguinating hemorrhage, however, selected diagnostic procedures are indicated if successful definitive measures are to be carried out. At the same time, a knowledge of the hazards involved is essential in arriving at a final decision concerning therapy, whether medical or surgical.

Any attempt to classify digestive-tract bleeding on the basis of the site of the lesion must be founded on a knowledge of anatomic and pathologic abnormalities encountered at various levels of the alimentary canal. This can be divided roughly into

three segments from the pharynx to the ligament of Treitz, from the ligament of Treitz to the ileocecal valve and from the ileocecal valve to the anus. A fourth possible subdivision includes the anal canal only.

In the upper segment — namely, the esophagus, stomach and duodenum — bleeding is usually associated with the vomiting of coffee-grounds material, inky-black fluid or frank blood. Even with esophageal bleeding, however, blood may not be vomited, and hemorrhage may be suspected only because of tarry stools. Melena is the rule in upper gastrointestinal-tract bleeding, but it must not be forgotten that feces containing currant-jelly-like, deep-reddish material may be encountered if the hemorrhage is brisk and the peristaltic rate rapid.

Esophageal bleeding is due either to varices or to cancer in most cases. Bleeding infrequently occurs from varices that are located in the fundus of the stomach rather than in the esophagus. Bleeding from esophageal ulcer can occur, but it is rare.

Gastroduodenal hemorrhage is usually due to peptic ulcers, the great majority of which are located in the first portion of the duodenum. Benign ulcers that bleed may occur, however, anywhere from the cardiac end of the stomach to the ligament of Treitz, and can be identified only by careful roentgenologic studies. Cancer of the stomach causes massive hemorrhage only occasionally, but it can do so. Less frequent causes of bleeding from the stomach are erosive gastritis, generalized or localized as in a diaphragmatic hernia, benign tumors that have become ulcerated and rare tumors, such as leiomyosarcomas, fibromas and neuromas. Carcinoma of the duodenum is extremely infrequent, but does occur and may cause bleeding. Duodenal leiomyosarcomas are more frequent and may underlie a serious anemia or may cause a fairly brisk hemorrhage.

It should be emphasized that gastritis alone is occasionally the source of an exsanguinating loss of

*The three papers comprising this symposium were presented at the annual meeting of the Massachusetts Medical Society, Boston, May 23, 1946.

†Clinical professor of medicine, Harvard Medical School physician, Massachusetts General Hospital.

sity 1941), research fellow in medicine, Bo Norberg, of Stockholm, Sweden (M.D. Karolinska Institutet, Stockholm, 1942) research fellow in physical chemistry, Herbert William Park, III, of Greensboro, North Carolina (S.B. University of North Carolina 1944, M.D. Duke University 1945), research fellow in physiology, Walter Pick, of Wingham, Connecticut (M.D. Harvard University 1942), research fellow in pediatrics, Hele Sinclair Pittman, of Cambridge (A.B. Smith College 1921, M.D. Johns Hopkins University 1927), instructor in medicine, Sam Madison Powell, of Waco, Texas (S.B. University of the South 1934, M.D. Tulane University 1938), assistant in pediatrics, Charles Edward Rath, Jr., of Cleveland, Ohio (A.B. College of Wooster 1940, M.D. Western Reserve University School of Medicine 1943), research fellow in medicine, Charles Washington Robertson, of Boston (A.B. Syracuse University 1935, M.D. Syracuse University 1939), assistant in surgery, Robert Rustigian, of Medford (S.B. Massachusetts State College 1938, S.M. Brown University 1940, Ph.D. Brown University 1943), research fellow in bacteriology and immunology, Harold Scheraga, of Brooklyn, New York (S.B. College of the City of New York 1941, A.M. Duke University 1942, Ph.D. Duke University 1946), research fellow in physical chemistry, Arnold Segel, of Cambridge (A.B. Harvard University 1932, M.D. Harvard University 1936), assistant in surgery, Nils Bengt Skanse, of Upsala, Sweden (M.D. University of Upsala 1945) research fellow in medicine, Lloyd Hollingsworth Smith, Jr., of Easley, South Carolina (A.B. Washington and Lee University 1944, medical student at Harvard from January 1944 to present) research fellow in physiology, Armando Soto-Rivera, of Caracas, Venezuela, South America (D.M. University Central de Venezuela 1943), research fellow in physiology, Herbert Carl Stoerk, of New York, New York (M.D. University of Vienna 1938) instructor in bacteriology and immunology, Melvin Irving Sturmick, of Allston (A.B. Harvard University 1935, M.D. Tufts College 1939), assistant in medicine, Yale Jerome Topper, of Cambridge (S.B. Northwestern University 1942, M.M. Harvard University 1943, Ph.D. Harvard University 1946), research fellow in biological chemistry, George Loughlin Tully, Jr., of West Newton (A.B. Boston College, 1941, M.D. Tufts College 1944), assistant in obstetrics, John Wily Garrett Tutthill, of Evanston, Illinois (A.B. Princeton University 1940, M.D. Harvard University 1943), research fellow in medicine, Bert Lester Vallee, of Brookline, Massachusetts (M.D. New York University 1941), research fellow in medicine, William Rhoads Waddell, of Tucson, Arizona (S.B. University of Arizona 1940, M.D. Harvard University 1943), research fellow in legal medicine, Roscoe Legrand Wall, Jr., of Winston-Salem, North Carolina (S.B. Wake Forest 1936, S.B. in medicine Wake Forest 1938, M.D. Jefferson Medical College 1940), assistant in obstetrics, Hans Heugh Wandall, of Copenhagen, Denmark (A.B. Oestere Borgerdydskole, Copenhagen, 1933, M.D. University of Copenhagen 1940), research fellow in surgery, George Wingate Waring, Jr., of Columbia, South Carolina (S.B. University of South Carolina 1940, M.D. Johns Hopkins University 1943), assistant in pediatrics, Stanford Wessler of Albany, New York (A.B. Harvard University 1938, M.D. New York University 1942), research fellow in medicine, LeMoyne White of Walpole, New Hampshire (A.B. Harvard University 1936, M.D. Harvard University 1940), assistant in psychiatry, Joan Hilma Whittaker, of Peterborough, Ontario (B.S. McGill University 1938) research fellow in obstetrics, James Paul Whittemore, of Somerville, Massachusetts (A.B. Holy Cross College 1942, M.D. Harvard University 1945), assistant in pediatrics, and Norman Zamcheck, of Swampscott (A.B. Harvard University 1939, M.D. Harvard University 1943), research fellow in legal medicine

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Haverhill, Massachusetts

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alimentary canal Specific toxic agents such as arsenite and radium may cause bloody diarrhea as a result of damage to the capillaries or bone marrow Not infrequently, similar symptoms occur in uremia, but only as a terminal event

It is thus obvious that a proper evaluation of gastrointestinal bleeding must include exact knowledge of the site of loss and, in addition, an understanding of the mechanism involved Without such an evaluation, therapeutic measures cannot be properly carried out It may be added that failure to obtain sufficient information to cover both requirements constitutes a failure of medical management and cannot be condoned Furthermore, it is essential to stress the fact that obvious sources of bleeding may not provide the actual explanation for hemorrhagic episodes Much too often the demonstration of hemorrhoids or anal fissures is accepted as a satisfactory explanation of rectal bleeding when the true cause is a carcinoma of the bowel or a serious ulcerative process

To obtain adequate information regarding the source and nature of gastrointestinal bleeding, carefully selected diagnostic procedures must be carried out If the hemorrhage is a massive one and shock is present or imminent, such measures must of necessity be brief and to the point They must not interfere with the immediate treatment needed for combating acute blood loss Blood volume must be restored at once by transfusions of whole blood, but this must not be administered so rapidly as to cause a sharp rise in blood pressure Gravity-drip, regulated transfusions are the measure of choice, and should be used until shock is controlled Plasma, which is of much less value than whole blood, should be used only when blood is unavailable An important reason for avoiding the use of pooled plasma, in addition to the fact that it does not replace hemoglobin and prothrombin, is that it carries a definite risk of transmitting the virus of infectious hepatitis Physiologic saline solution should be used only as a temporary expedient until whole blood can be obtained In the presence of protein or albumin lack, such as that occurring in depleted patients or in serious hepatic disease, the use of saline solution may precipitate the appearance of pulmonary edema or generalized tissue edema

During the period of shock therapy, certain valuable diagnostic information can be obtained A history of previous ulcer may be elicited from the family or friends or from the patient Evidence of emaciation may suggest the presence of cancer Spider angiomas may lead to an immediate diagnosis of portal hypertension, with esophageal or gastric varices The presence of jaundice may incriminate the liver Light percussion may demonstrate splenic enlargement and lead to a similar conclusion Inspection may reveal an abdominal mass necessitating an obvious diagnosis of cancer Abdominal palpation must be done with caution, if

at all, but may yield diagnostic information A careful digital examination may reveal a tumor mass in the rectum, immediately indicating the diagnosis

As soon as the danger of shock has been successfully met or it is apparent that major bleeding is not present, more intensive diagnostic measures can be instituted These should be carried out in the following order a searching history, a thorough physical examination, careful roentgenologic studies, — discussed and planned according to the findings of the history and physical examination, — endoscopy and a few laboratory tests A meticulous history alone may indicate the segment to be studied even if a positive diagnosis cannot be made Substernal epigastric symptoms imply upper-segment disease, periumbilical pain suggests the small intestine as the source of bleeding, discomfort in the right lower quadrant should lead to examination of the ileocecal region, and hypogastric distress suggests colonic disease Positive physical findings may be diagnostic, but they are often notable for their absence A palpable mass means cancer until proved otherwise by direct inspection In most cases, the indicated roentgenologic studies, without manipulation, should be carried out within twenty-four to forty-eight hours of the occurrence of massive bleeding

Gastroscopy, esophagoscopy and sigmoidoscopy should be postponed until active bleeding ceases The indications for their use are clear In the absence of definite roentgenologic findings, or when supplemental evidence regarding the nature of the bleeding lesion is desirable, endoscopic examination should be performed as soon after major bleeding has ceased as it can safely be done Sigmoidoscopic examination should precede roentgenologic study It may give more accurate information than a barium enema — in mild ulcerative colitis, for example Similarly, it may reveal a polyp or a cancer that is difficult to demonstrate roentgenologically In the presence of hemorrhoids or an anal fissure, sigmoidoscopy is essential to rule out a more serious source of bleeding at a higher level With bleeding obviously arising from the lower digestive tract, a negative sigmoidoscopy immediately provides the proper impetus for a serious roentgenologic study of the upper colon and terminal ileum

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blood. It is also essential to remember that massive hemorrhage from ulcer is frequently unassociated with pain.

In the midsegment — the jejunum and ileum — massive hemorrhage is rather rare, but anemia from chronic loss of relatively small amounts of blood is not infrequent. Hematemesis does not occur from lesions below the ligament of Treitz, except in the presence of frank obstruction with fecal vomiting, or in association with an ulcerated lesion near the stoma of a gastroenterostomy. Dependent on the peristaltic rate, bleeding from the midsegment may result in either tarry stools or fresh, blood-stained feces.

Acute bleeding may result from frank ulceration, such as that encountered in typhoid fever, or from a single ulcer, notably that associated with a Meckel's diverticulum, which is usually, but not invariably, seen in children and young adults. Tumors, unless pedunculated and therefore subject to torsion, do not, as a rule, cause massive bleeding. Rather, they result in a gradually progressive anemia due to ulceration and oozing. Carcinomas, leiomyosarcomas, lymphomas and benign polypoid tumors, such as simple adenomas and lipomas, cause bleeding that may or may not be associated with the clinical picture of intussusception. With modern methods of roentgenologic examination, the site of the bleeding in the small intestine is often demonstrated if its approximate location is suspected. Other sources of moderate bleeding in this portion of the bowel are the granulomatous processes, notably tuberculosis and regional enteritis, both of which tend to be located in the vicinity of the ileocecal valve. Acute infectious processes, such as food poisoning and gastroenteritis due to what is popularly known as "intestinal gripe," may cause moderate bleeding from the small intestine.

Bleeding in the colon, which may be due to a wide variety of conditions, is demonstrated by the passage of varying amounts of fresh or slightly altered blood in the stools. Cancer must be suspected first, last and always in the presence of colonic bleeding. Until it is eliminated no other diagnosis should be considered. Carcinoma of the colon may cause gross, shock-producing hemorrhage, but as a rule effects a more chronic blood loss resulting in an anemia that may be serious. Other tumors are the source of intermittent fresh bleeding. Of these, in the absence of signs of serious disease, the adenomatous polyp, which is always potentially cancerous, should be the first suspect.

If carcinoma and adenoma can be ruled out, colonic bleeding should suggest the possibility of one of the various forms of ulcerative colitis. If the onset is abrupt, amebic and bacillary dysentery must be eliminated by appropriate diagnostic measures. Tuberculous colitis and idiopathic ulcerative colitis are usually more insidious in onset and more chronic in their clinical manifestations

but, like the dysenteries, are accompanied diarrhea.

An important cause of serious colonic bleed may be the end result of damage to the b secondary to heavy irradiation of pelvic tun. Rarely, bright-red blood may be passed by rec from areas of diverticulitis or in the presenc mucous colitis. Such a possibility should neve considered until all other sources of bleeding h been eliminated, and even then it should be accep only with extreme skepticism.

I have enumerated many of the possible sou of gastrointestinal hemorrhage on the basis o strict anatomic or pathologic location. It is equ necessary to visualize the type of mechanism involved in the hemorrhage. This is particularly vi in arriving at the details of therapeutic managem involved in any given case. For example, the ble ing from a peptic ulcer is essentially arterial a therefore has a graver prognosis at the age of six than at thirty, owing to the fact that the arteri are less elastic, contract less well and, in additio may carry a high systolic pressure. Bleeding fro varices, on the other hand, is from a thin-walle relatively atonic vessel that is easily traumatize and has little contractility but has great possibilit of thrombosis and obliteration by clot formatio. The hemorrhage secondary to a mesenteric-arter thrombosis carries with it the added threat of ga grene of the bowel and therefore the possible neces sity of emergency surgery.

Capillary bleeding may occur over a large enoug area to provide an immediate threat to life, al though, as a rule, it is of lesser magnitude. The bleeding from gastritis, either diffuse or localized, and that encountered in idiopathic ulcerative colitis are usually of capillary origin. Similarly, in bacillary dysentery, bleeding is the result of tiny, superfical mucosal erosions involving capillary loops. In diverticulitis and so-called "mucous colitis," the infrequent episode of bleeding is probably due to a local inflammatory process with involvement of a small vessel. In hemorrhage secondary to post radiation lesions of the sigmoid or ileum, the bleed ing comes from telangiectatic areas similar to those noted in the skin following x-ray burns but because of the larger vessels involved, may be of greater degree than that usually noted in capillary oozing and may require local surgical resection.

Significant hemorrhage, essentially of capillary origin, may be due to general hemorrhagic disturbances associated with the thrombocytopenia encountered in the leukemias and bone-marrow aplasias, or with the prothrombin lack associated with serious hepatic disease or chronic diarrhea. Vitamin C deficiency may provide the basis for blood loss from the digestive tract from capillary oozing. Similarly, serious capillary bleeding may be due to hemophilia, but this is only a manifestation of a general physiologic disorder affecting more than the

imentary canal. Specific toxic agents such as acetone and radium may cause bloody diarrhea as a result of damage to the capillaries or bone marrow. Not infrequently, similar symptoms occur in uremia, but only as a terminal event.

It is thus obvious that a proper evaluation of gastrointestinal bleeding must include exact knowledge of the site of blood loss and, in addition, an understanding of the mechanism involved. Without such an evaluation, therapeutic measures cannot be properly carried out. It may be added that failure to obtain sufficient information to cover both requirements constitutes a failure of medical management and cannot be condoned. Furthermore, it is essential to stress the fact that obvious sources of bleeding may not provide the actual explanation for hemorrhagic episodes. Much too often the demonstration of hemorrhoids or anal fissures is accepted as a satisfactory explanation of rectal bleeding when the true cause is a carcinoma of the bowel or a chronic ulcerative process.

To obtain adequate information regarding the source and nature of gastrointestinal bleeding, carefully selected diagnostic procedures must be carried out. If the hemorrhage is a massive one and shock is present or imminent, such measures must of necessity be brief and to the point. They must not interfere with the immediate treatment needed for combating acute blood loss. Blood volume must be restored at once by transfusions of whole blood, but this must not be administered so rapidly as to cause a sharp rise in blood pressure. Gravity-drip, regulated transfusions are the measure of choice, and should be used until shock is controlled. Plasma, which is of much less value than whole blood, should be used only when blood is unavailable. An important reason for avoiding the use of pooled plasma, in addition to the fact that it does not replace hemoglobin and prothrombin, is that it carries a definite risk of transmitting the virus of infectious hepatitis. Physiologic saline solution should be used only as a temporary expedient until whole blood can be obtained. In the presence of protein or albumin lack, such as that occurring in depleted patients or in serious hepatic disease, the use of saline solution may precipitate the appearance of pulmonary edema or generalized tissue edema.

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at all, but may yield diagnostic information. A careful digital examination may reveal a tumor mass in the rectum, immediately indicating the diagnosis.

As soon as the danger of shock has been successfully met or it is apparent that major bleeding is not present, more intensive diagnostic measures can be instituted. These should be carried out in the following order: a searching history, a thorough physical examination, careful roentgenologic studies, — discussed and planned according to the findings of the history and physical examination, — endoscopy and a few laboratory tests. A meticulous history alone may indicate the segment to be studied even if a positive diagnosis cannot be made. Substernal epigastric symptoms imply upper-segment disease, periumbilical pain suggests the small intestine as the source of bleeding, discomfort in the right lower quadrant should lead to examination of the ileocecal region, and hypogastric distress suggests colonic disease. Positive physical findings may be diagnostic, but they are often notable for their absence. A palpable mass means cancer until proved otherwise by direct inspection. In most cases, the indicated roentgenologic studies, without manipulation, should be carried out within twenty-four to forty-eight hours of the occurrence of massive bleeding.

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Laboratory tests are of much less diagnostic importance than the measures discussed above in determining the source or nature of gastrointestinal bleeding. The finding of histamine achlorhydria in the presence of a demonstrated gastric lesion is of

value because it implies cancer as the underlying cause. Otherwise, gastric analysis is a needless procedure in the problem under discussion. When bleeding is due to a blood dyscrasia, such as thrombocytopenia, proper blood studies are obviously diagnostic. A prothrombin lack can be demonstrated only by a prothrombin determination, but decision regarding the underlying cause of blood loss is usually made by simple clinical observation, which is then confirmed by the appropriate laboratory test. In the main, laboratory findings are of aid only in demonstrating and measuring the effects of hemorrhage and in thus giving direction and timing to the proper treatment to correct blood loss.

The therapy of gastrointestinal hemorrhage is twofold. Immediate treatment has already been mentioned. It should be straightforward, adequate and continued until the pressing hazard of shock has been controlled, or until it is obvious that bleeding is not subsiding. In the latter event, a decision must be made for emergency surgical intervention. Subsequent therapeutic measures must be equally straightforward and directed toward obtaining medical control of the cause of bleeding or surgical removal of its source. When cancer is suspected or proved, radical surgical procedures must be instituted as soon as proper preoperative preparations to combat anemia, depletion, specific vitamin lack and the like have been carried out. In the presence of a proved peptic ulcer not requiring emergency surgery, simple feeding measures should be started early, and moderate sedation achieved. In my opinion, morphine should not be used because of its tendency to cause nausea and abnormal duodenal spasm, it is not a sedative, and barbiturates are more satisfactory. The current suggestion for the feeding of amino acid preparations may be useful in extremely malnourished patients, but simple, less distasteful feedings are usually preferable. Antacids may be helpful, and atropine may also be used to advantage either by mouth or parenterally. Iron should be avoided until all ulcer activity has ceased, because of its frequent irritating effect on the gastrointestinal tract. Transfusions, once the hemoglobin is at a safe level, are not needed and are probably inadvisable. After the bleeding episode has been

successfully managed, proper elective surgery is usually indicated if the hemorrhage has been major one. There are occasional exceptions to such a decision.

In bleeding from esophageal varices, feeding should be delayed because of the danger of further trauma to a ruptured varix. Because bleeding from this source is usually secondary to severe liver disease, transfusions or vitamin K or both are indicated for the additional purpose of correcting a bleeding tendency due to prothrombin lack.

Treatment of hemorrhage from gastritis is essentially the same as that from ulcer. If there has been prolonged vomiting, however, intravenous feeding must be utilized as a temporary expedient to replace fluid and electrolytes and to prevent gastric irritation. When massive bleeding occurs as a result of a local gastritis or an ulcer in a diaphragmatic hernia, medical treatment should usually be followed by elective transthoracic surgery aimed at repairing the hernia.

I shall mention only one other specific cause of bleeding — namely, ulcerative colitis. In this distressing condition, bleeding occasionally dominates the clinical picture. If intensive medical therapy does not control the blood loss in a reasonable and limited period, it is imperative that a decision be made for adequate surgical measures — ileostomy or colectomy, depending on which maneuver is indicated in the individual case.

Bleeding from direct trauma, which obviously falls into a separate category, is not considered

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In this review of gastrointestinal bleeding as seen by the internist, I have tried to stress certain important points, none of which are new. Determination of the site and character of the hemorrhage — that is, exact diagnosis — is essential to proper, detailed therapeutic measures. Treatment must be directed toward immediate control of the sequelae of massive hemorrhage and subsequently toward adequate cure or management of the underlying cause. To achieve satisfactory results, the close cooperation of a well trained roentgenologist and of a competent surgeon is essential.

THE SURGICAL ASPECTS OF HEMORRHAGE FROM PEPTIC ULCER*

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A STUDY of the patients who have entered the surgical wards of the New York Hospital with serious hemorrhage from the gastrointestinal tract shows that the large majority were the victims of duodenal or gastric ulcer, whereas a minority presented a variety of other pathologic conditions. I was asked to discuss the large subject of hemorrhage from the gastrointestinal tract in its relation to surgery, but since it is obvious that I cannot cover so large a field in the short time at my disposal, I shall confine myself to the surgical aspects of hemorrhage from peptic ulcer, which, in my experience far overshadows in importance the others.

In reviewing this experience I find that of over 1800 patients with duodenal and gastric ulcer admitted to the surgical wards between September 1, 1932, and January 1, 1946, a total of 337 were admitted specifically because of serious hemorrhage. These cases have been reviewed from time to time. Holman,¹ in an analysis of the first 90 cases of serious hemorrhage, observed that 12 patients died, a mortality from hemorrhage of 13 per cent. In this group, 4 patients were in such a desperate condition that operation was never considered possible, 4 were operated on as a last resort, 4 recovered to a point where operation could have been performed but surgery was delayed, with the result that they died from a second massive hemorrhage. On the other hand, 4 patients operated on during active bleeding recovered. This experience shows that 8 patients in whom operation was not undertaken died from hemorrhage and that of 8 subjected to operation as a desperate venture, 4 recovered and 4 died — a surgical mortality of 50 per cent. Of the 74 patients who recovered from the primary hemorrhage under expectant treatment, 16 had been subjected to gastric resection at the time of the report and all had recovered.

Holman² subsequently studied 161 patients with severe hemorrhage admitted between 1932 and 1940, including the 90 referred to above. In this series there were 18 deaths during the period of active bleeding, a mortality from hemorrhage of 11 per cent. Thirteen patients died without having been subjected to surgery. Fourteen patients were operated on in the period of active bleeding, with 5 deaths — a surgical mortality of 35 per cent. Of the 134 patients who recovered from the primary hemorrhage under expectant treatment, 31 had been subjected to gastric resection at the time of the report, with 1 death — a mortality of 3 per cent.

Clifton,³ beginning where Holman left off, added 103 patients with serious hemorrhage admitted between July 1, 1940, and July 1, 1943. In this series there were 5 deaths during the period of active bleeding, a mortality from hemorrhage of less than 5 per cent. Three patients could not be brought into condition for operation and died two hours, eight hours and five days, respectively, after admission. Operation was performed in 8 cases during the period of active bleeding, with recovery in 6 and death in 2 — a surgical mortality of 25 per cent. Of the 92 patients who recovered from the primary hemorrhage, 41 had been subjected to gastric resection at the time of the report, with 2 deaths — a surgical mortality of 5 per cent.

Cooper,⁴ in a study of 73 patients with serious hemorrhage admitted since Clifton's report and covering the period from July 1, 1943, to January 1, 1946, found a total of 5 deaths, only 4 of which could be related to hemorrhage, however. This represents a mortality from hemorrhage of 5 per cent. Two patients died from hemorrhage without having been subjected to operation. Nine patients were operated on in the period of active bleeding — of whom 7 had gastric resections — with 2 deaths, a surgical mortality of 22 per cent. Of the 62 patients who recovered from the primary hemorrhage 33 were subjected to operation within four to six weeks, of whom 30 were subjected to gastric resection, 1 to a gastroenterostomy, 1 to a ligation of the gastric artery and 1 to an exploratory laparotomy. There was 1 postoperative death, an operative mortality of 3 per cent. As of January 1, 1946, there were 29 patients who had not been subjected to operation.

In summary, of 337 patients with peptic ulcer admitted to the hospital because of serious or massive hemorrhage, 27 (8 per cent) died from hemorrhage. Eighteen died without having been subjected to surgery, in the majority of cases the condition of the patient precluding, in the judgment of the surgeon, an operative procedure. Thirty-one patients were operated on in the period of active primary hemorrhage, with 9 postoperative deaths — a surgical mortality of 29 per cent. From the location of the ulcer and the source of bleeding it is probable that all 31 patients would have died had surgery not been undertaken. It thus appears that 49, or 15 per cent, of the total number of patients admitted because of severe hemorrhage were examples of fatal hemorrhage, a higher percentage than is usually appreciated.

Of the 288 patients who recovered from hemorrhage under expectant treatment, 105 were sub-

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jected to operation at the time of the reports mentioned above. The operation was, with few exceptions, a gastric resection with removal of the ulcer — and was performed usually within four to six weeks after the primary hemorrhage. There were 4 post-operative deaths, a case mortality of 4 per cent. The remaining 183 patients were discharged from the hospital to be followed in the clinic.

From the 18 patients who died without operation, in whom permission for autopsy was obtained in a high percentage of cases, from the 31 subjected to operation during the period of active bleeding and from the 105 patients operated on within four to six weeks after recovery from the hemorrhage that led to admission, a total of 154 cases, it has been learned that the location of the ulcer with reference to immediately adjacent large arteries is the determining factor in the seriousness of or fatality from hemorrhage. Without exception the duodenal ulcers with hemorrhage that was fatal or unchecked by a conservative regimen were located on the posterior duodenal wall and had eroded the pancreaticoduodenal artery or one of its major branches, if gastric, the ulcers were on the lesser curvature, eroding a large branch of the right or left gastric artery. The pathologic picture was strikingly similar in all cases: the ulcer was deep and presented a hard, fibrous base in which there was an eroded, open artery whose lumen, in some of the specimens at autopsy, was large enough to admit a matchstick. In this series the ulcer that gave rise to fatal hemorrhage, if unchecked by surgery, was located in one or the other of the two areas indicated and was usually chronic, and the hemorrhage was arterial and more frequently from a single eroded artery.

At operation performed during the period of bleeding, a conical clot temporarily stopped the bleeding from even a large eroded artery, but I have also observed how easily such a clot may be dislodged and how unlikely it is to become organized and fixed. It is not implied from these statements that hemorrhage from ulcers of the posterior wall of the duodenum or lesser curvature may not, under a medical regimen, spontaneously cease, for it is of course the size of the blood vessel eroded that is the determining factor. The ulcers with hemorrhage that was checked under a conservative regimen were in most cases located away from the two dangerous vascular areas described above or, if located in those areas, had not eroded a large artery. It is the early, acute and not deeply penetrating ulcers — those of the anterior wall of the duodenum and those of the distal portion of the lesser curvature and fundus of the stomach — that give rise to less dangerous hemorrhages.

It is evident from this experience that in any series of patients with serious hemorrhage as the primary cause of admission to the hospital, there will be two groups — a minority, in whom hemorrhage, if not surgically checked, is fatal, and a

majority, in whom hemorrhage, under expectant treatment, spontaneously ceases. In our experience the former group varied in different periods from 18 to 11 per cent of the total, averaging about 1 per cent. No doubt this percentage varies in different clinics, but it is evident from the literature that surgical clinics quite generally have a minority group of greater or lesser size to contend with.

The immediate clinical problem is accurately to differentiate the group whose hemorrhage is uncontrollable short of surgical measures and that whose hemorrhage ceases under conservative measures. The immediate surgical problem is how, in patients with uncontrollable hemorrhage, to arrange all details of a surgical procedure so as to save the greatest number of lives. A third, but not so immediate problem, is how most intelligently to care for the majority group, who have recovered from hemorrhage under expectant treatment.

The differentiation of patients whose hemorrhage is likely to prove fatal if unchecked by surgery and those in whom it ceases under a proper conservative regimen has proved extremely difficult. Patients are admitted in all stages of reaction to hemorrhage. Some are in such a desperate condition that they die in the emergency unit before they can be transferred to the wards, in spite of large or repeated small blood transfusions. Others less profoundly affected show great variations in their reactions to hemorrhage, as manifested by physical appearance, pulse rate, respiration, blood pressure, sweating, mental state, blood counts and hemoglobin determinations. It is well known that patients react differently to the loss of blood and that unless some accurate data can be obtained regarding the amount of blood vomited or passed by rectum, it may not be known on admission of the patient how large a hemorrhage has taken place. Moreover, the clinical picture presented cannot immediately reveal whether the hemorrhage is derived from an eroded pancreaticoduodenal artery and will continue, proving fatal if unchecked, or whether it is derived from an ulcer in a less dangerous location and will cease under a conservative regimen. It is a question whether one should attempt, in the early period of observation, to establish the location of the ulcer and thus clarify the situation regarding therapy. In many patients, attempts at gastroscopy are unwise and impossible, a swallow or two of barium, with observation under the fluoroscope, had tragic consequences in 3 cases, being promptly followed by a fatal secondary hemorrhage. It appears logical, in all the circumstances, to attempt to differentiate patients whose hemorrhage is likely to prove fatal and those whose hemorrhage is likely to cease spontaneously by following the early clinical course under appropriate treatment — that is, to put them to bed, to administer moderate doses of morphine to induce quiet, to withhold food

and fluids by mouth, to supply fluids by vein and to give adequate blood transfusions

If such a practice is followed, the response to these measures falls into two main groups: some patients merely hold their own and do not improve or they continue to fail, for they are still bleeding and the blood escapes from the open artery in the base of the ulcer as rapidly as or more rapidly than it is introduced into the veins; others improve, as evidenced by physical appearance, pulse, blood pressure and other favorable signs. With the latter, it may be assumed that the hemorrhage had ceased at the time of admission or, if continuing, has greatly decreased. The fact that these patients improve is not positive proof that the hemorrhage was not derived from an open pancreaticoduodenal or major branch of the right or left gastric artery, for under a strict regimen, as indicated above, some patients suffer a second massive or even fatal hemorrhage in the next two hospital weeks; this may occur spontaneously or may be initiated by the administration of food or a swallow of barium with the purpose of localizing the lesion. Of all the criteria assembled to differentiate the cases of hemorrhage that are likely to prove fatal, the failure of hemorrhage to stop under a strict medical regimen and the recurrence of hemorrhage after it has temporarily stopped and while the patient is on a strict medical regimen are the most positive. In all cases that exhibited these manifestations the ulcer was located on the posterior wall of the duodenum, implicating the pancreaticoduodenal artery, or on the lesser curvature of the stomach, involving a large branch of the gastric artery. In passing I may say that these statements also apply to patients admitted not because of hemorrhage but because of other symptoms of ulcer who, while under a strict medical regimen, have a serious hemorrhage.

It therefore appears that among patients admitted because of serious hemorrhage there will be some — in the experience cited above, 15 per cent of the total — who die of hemorrhage that is not surgically checked. The most positive indications of such hemorrhage are the failure of improvement under a strict medical regimen, including adequate blood transfusions, with or without evidence of continuing bleeding, such as the vomiting of blood and the passage of blood by rectum, and the recurrence of hemorrhage under a strict medical regimen. Patients who present these indications must seriously be considered subjects for early operation, for otherwise a high percentage will die.

Other factors affect the seriousness of hemorrhage in ulcer. Age has been shown to be a factor by a number of authors, and the experience discussed above supports the view that hemorrhage is likelier to be serious and fatal in patients over fifty years of age. This is due not only to the higher incidence of arteriosclerosis but also to cardiorenal complications. Sex is also a factor, and it is well known that

fatal hemorrhage is less frequent in women than in men.

Thus far in my discussion I have tried to define and segregate patients with serious or massive hemorrhage in whom immediate or early operation must seriously be considered. What are the criteria in arriving at a prompt decision to operate? I have referred to patients who are admitted in profound shock and, judged by the usual criteria, present every contraindication to operation. Should operation be delayed, in the hope that the patient will improve and be less grave a surgical risk, or should contraindications be disregarded and a desperate surgical venture undertaken? Both methods of approach to the problem have been tried. Whether operation is performed early or delayed, a fairly high mortality can be expected. The question is, Which will achieve the lower mortality? From this admittedly limited experience, early operation appears to be the better choice. The principle — established in wounds of war and accidents of civil life — that active hemorrhage must be controlled before progress can be made toward saving life is equally applicable in the type of hemorrhage under discussion. In exposing an ulcer of the posterior duodenal wall with an eroded, actively bleeding, pancreaticoduodenal artery, I have not only been amazed at the amount of blood that can be poured into the duodenum in a short time but also struck with the futility of blood transfusions as a means of saving life until the bleeding vessel has been controlled.

The question of when to operate in this particular group of cases has been discussed by a number of authors, and it appears that early operation — within twenty-four to forty-eight hours after the onset of hemorrhage — will save more lives. Finsterer,³ an advocate of operation for massive hemorrhage in chronic ulcer, reports that in 59 patients operated on immediately or within forty-eight hours the mortality was 5 per cent, whereas in 53 operated on late it was over 30 per cent. Gordon-Taylor,⁶ Oliani⁷ and others also found that early operation gave better results. The experience in this hospital shows that of 21 patients operated on early, 2 died — a mortality of 10 per cent — and that of 10 operated on late, 7 died — a mortality of 70 per cent. The experience quoted indicates that operation should be promptly decided on and executed.

After operation has been decided on, one of the most important factors in a successful outcome is an unlimited amount of blood available for transfusion. The introduction of blood, previously begun in the ward, should be continued throughout the operation and after operation, according to indications. The treatment of the wounded in war demonstrated the value of large amounts of whole blood in patients with massive and continuing hemorrhage, and the situation in hemorrhage from ulcer is similar. The primary object of surgery is to con-

trol hemorrhage and save life, the treatment of the ulcer from an immediate viewpoint is secondary, as it is in acute perforation. The operative procedure of choice, then, should be the quickest and simplest that will completely control hemorrhage.

For both duodenal and gastric ulcers, the operations performed include the following: the local ligation of the artery in the base of the ulcer by an encircling ligature, the ligation of the artery or arteries outside the visceral wall, the local excision of the ulcer with the control of hemorrhage, with such additional procedures as may be necessary to re-establish the continuity of the gastrointestinal tract, and gastric resection, including the bleeding ulcer. Experience with these procedures shows that they all have some disadvantages. Local ligation of the bleeding vessel in the base of the ulcer and the ligation of vessels outside the visceral wall have not proved uniformly successful. A continuation of the ulcerative process or the cutting through of ligatures or their combination may result in a recurrence of hemorrhage during the first or second week after operation. In ulcers high on the lesser curvature of the stomach, experience with these two procedures has been particularly unfavorable. Because the lesions were so high as to encroach on the esophagus, neither local excision nor any other procedure appeared feasible. In 3 patients with lesions of this sort, hemorrhage was temporarily checked but recurred and resulted in death. Post-mortem examination showed further erosion and reopening of the blood vessels. Local excision of the ulcer with the control of hemorrhage is definitely a safer procedure from the viewpoint of permanently controlling hemorrhage. In lesions favorably situated, it can be done almost as rapidly as the preceding two procedures. In lesions of the stomach and duodenum adjacent to the pylorus, the excision of the ulcer and the necessary repair may occlude the stomach or duodenum and make necessary an additional procedure, such as a pyloroplasty or a gastroenterostomy, which prolongs operation and adds to its hazards in a depleted patient. Gastric resection with removal of the ulcer is the most formidable operation for dealing with the situation. Its duration and often its technical difficulties are disadvantages. If it succeeds, there is in addition to saving life the greater probability of curing the patient of the disease.

These are the most frequent methods of surgical treatment of the bleeding ulcer. It is apparent that rules for their use cannot be stated. The judgment of the surgeon must guide him in determining which procedure he will use in an individual case. Generally speaking, however, it can be said that local attempts at controlling hemorrhage without removal of the ulcer are the least safe of the methods of permanently controlling hemorrhage.

As I have indicated above, approximately 15 per cent of patients who enter the hospital with massive

hemorrhage die unless they can be saved by prompt surgery. Eighty-five per cent, under a careful medical regimen, including blood transfusions, recover from the hemorrhage for which they are admitted. What should the policy toward this group of patients be? As pointed out above, of 288 patients who recovered from their primary hemorrhage, 105 were subjected to operation — the large majority, to gastric resection — within four to six weeks after the primary admission for hemorrhage. There were 4 postoperative deaths, a mortality of 4 per cent. One hundred and eighty-three patients had not been operated on at the time the various studies were made but had been discharged from the hospital to be followed in the clinic.

I had hoped to be able to report the follow-up studies on the entire series of cases, but I could not complete the task in time for this meeting. I am, however, able to report on the group of 73 cases occurring between July 1, 1943, and January 1, 1946, in which 2 patients died without operation, 9 were operated on during the period of active hemorrhage, with 7 recoveries and 2 postoperative deaths, 33 were subjected to operation within four to six weeks after recovery from the hemorrhage for which they were admitted and 29 were not subjected to operation but were discharged to be followed in the clinic.

Of the 7 survivors among the 9 patients subjected to operation during the period of active hemorrhage all were subjected to gastric resection, with satisfactory results from the primary resection in 6. One had a poor result but was subjected to a second resection with a satisfactory result. The results were therefore satisfactory in this group.

Of the 33 patients subjected to operation within four to six weeks after recovery from the primary hemorrhage, 25 had primary gastric resections, 5 had secondary resections (these patients had previously been operated on), 1 had a gastroenterostomy, 1 had a ligation of the left gastric artery, and 1 had an exploratory laparotomy.

Of the 25 patients with primary resections, 1 died after operation. Of the 24 survivors, 21 at present have satisfactory results and 3 have poor results, the 3 patients with poor results have developed recurrent ulceration, with recurrent hemorrhage, but all are living at the present time.

Of the 5 patients with secondary gastric resections, 3 have satisfactory results at present. The 2 with poor results developed recurrent ulceration with hemorrhages — both were subjected to further gastric resections and both still have poor results, with recurrent hemorrhages, but are alive.

The patient subjected to gastroenterostomy has at the present time a satisfactory result. The patient subjected to ligation of the left gastric artery had a poor result, with recurrent hemorrhages. He was subjected to a gastric resection during active bleeding, with a satisfactory result at present. The patient

subjected to exploratory laparotomy without the discovery of a demonstrable active ulcer has a poor result, with recurring hemorrhages. He is living at the present time.

In summarizing this group of 33 patients it appears that they have been subjected to thirty-five operations (thirty-three gastric resections) in attempts to control hemorrhage and to prevent recurrent ulceration. There was 1 postoperative death — an operative and case mortality of 3 per cent. Of the survivors, 26 (81 per cent) have satisfactory results at present and 6 (19 per cent) have poor results with recurring hemorrhages. Gastric resection, in this group, was effective in controlling hemorrhage and preventing recurrent ulceration in 84 per cent of the cases.

Of the 29 patients discharged from the hospital without having been subjected to operation, 28 have been successfully followed. Of these, 24 have a satisfactory result from the viewpoints of both absence of recurrent hemorrhage and relief from other ulcer symptoms. Four with poor results have had recurrent hemorrhages but are living. Under a careful medical regimen, therefore, the results were satisfactory in 85 per cent of these patients.

I am unwilling to draw any definite conclusions from these data. The follow-up period is too short, for the majority of patients have been followed less than three years. From all the studies on ulcer that I have made it is evident that accurate statements regarding the effectiveness of either medical or surgical measures cannot be made on the basis of a follow-up period of less than five years, and I must add that statements based on such a follow-up period must be modified in the years that follow. Again, the data that I have presented cover only a part of the entire series, a complete study of which may show results at variance with those given. From such data as I have on the entire series, it appears that 37 per cent of these patients were subjected to early gastric resection (within four to six weeks) and that 63 per cent were treated medically. From observations admittedly incomplete I find that gastric resection, after a relatively short follow-up period, assures control of hemorrhage and prevention of recurrent ulceration in 84 per cent of cases, with a primary surgical mortality of 3 per cent. I find, also, that on the basis of a similar short follow-up period, a medical regimen may yield highly satisfactory results in selected cases. I have no positive evidence that every patient who bleeds must necessarily be subjected to surgery. But there is evidence that a certain percentage of cases should be subjected to early surgery. First, it is known that hemorrhage, with the exception of acute perforation, is the most frequent cause of death in ulcer. Secondly, it is known that although acute ulcers may give rise to serious hemorrhage, the deeply penetrating, more chronic ulcers oftener cause dangerous and fatal hemorrhage — perhaps I should

use the term "actively penetrating" rather than "chronic ulcer," for Holman et al.⁸ found that in older patients the increased mortality from hemorrhage does not bear a relation to the age of the ulcer, since the average duration of symptoms was slightly over four years in those who recovered from hemorrhage and four years in those who died. Thirdly, age, in the experience discussed above and in that of a number of authors, is a factor, more patients forty-five to fifty years of age and over being likely to suffer hemorrhages leading to death than patients in younger age groups. The higher death rate in the older age groups is not wholly due to the hemorrhage but in part to a higher incidence of complications caused by loss of blood, particularly cardiorenal complications. Again, the repetition of hemorrhage is believed by some to be of importance in determining treatment. Jordan and Kiefer,⁹ for example, found that 70 per cent of patients who had two or more hemorrhages suffered further hemorrhages. And finally, Holman¹⁰ and others have noted that patients with chronic ulcer and with a history of present or past hemorrhage do not do well under a medical regimen and are prone not only to a continuation of pain and other symptoms but also to recurrent hemorrhage. This finding is not supported by the follow-up studies in the small group of 28 cases considered above, who were not followed for a sufficiently long period of time, however.

Although these observations have a bearing on the problem of treating patients who have recovered from the hemorrhage that brought them to the hospital, it must be admitted that they are somewhat vague to be formulated into a clear-cut policy. Any policy for this group of patients cannot well be determined on the basis of hemorrhage alone, it must include consideration of the ulcer and its duration, location, pathologic characteristics and probable tendency to heal. If a patient has suffered a serious hemorrhage and harbors an ulcer that experience indicates is unlikely to respond to a medical regimen, the occurrence of hemorrhage is an added reason for surgical therapy, if experience suggests that the patient has an ulcer that is likely to respond to a medical regimen, a first or second hemorrhage should not weigh too heavily in the decision to recommend early surgery. Until more clear-cut information is available, the decision regarding therapy in this group of cases must rest on the consideration of all the factors enumerated. If surgery is decided on, gastric resection, with invariable removal of the ulcer if possible, is the operation of choice, although it does not necessarily protect the patient against either subsequent ulceration or hemorrhage.

This discussion has been confined to hemorrhage in patients with peptic ulcer. I should, perhaps, refer to a related group of patients who have massive and sometimes fatal hemorrhage but who fail to present a demonstrable ulcer. This group of patients has

been a particularly discouraging one. Pathologically, the information regarding the source or sources of hemorrhage has been meager. At autopsy the pathologist has, generally speaking, failed to find an ulcer or other causes of hemorrhage. In one case the pathologist did not find even an erosion of the mucosa of the stomach and duodenum, but when the gastric artery was connected with a pressure bottle of salt solution a jet of fluid was projected from the mucosa. The area was excised, and serial sections showed a small ruptured aneurysm covered by intact mucosa. At operation in these cases the most careful inspection and palpation of the stomach and duodenum fails to demonstrate an ulcer. In some of these cases the stomach has been opened by a long incision parallel with the greater curvature, the stomach literally turned "inside out" and the entire mucosa not only of the stomach but also of the proximal duodenum carefully examined, without the demonstration of an ulcer. In the majority of cases so examined the bleeding temporarily ceased and a source of hemorrhage was not found. Yet within a week the patient may suffer another devastating hemorrhage.

Clinically patients suffering from this type of hemorrhage often fail to present any symptoms that serve to differentiate them from those with ulcer, although a clear-cut history of ulcer may be absent. The first hemorrhage may be fatal, and the assumption is that the patient has bled from an ulcer until autopsy proves otherwise. Again, patients may have repeated hemorrhages from which they recover under appropriate treatment. A patient of one of my associates whom I saw in consultation had fifty-eight massive hemorrhages over a period of twenty-five years and had been admitted to and carefully studied in many of the important clinics throughout the country. He had been operated on in one clinic and a gastric resection performed even though an ulcer was not demonstrated. He entered the New York Hospital exsanguinated from his fifty-ninth hemorrhage. He recovered and was again operated on because of the suspicion of a duodenal ulcer. A further segment of duodenum was resected, but an ulcer was not found. After having shown such a tenacity of life for so many years, it seems a pity that the patient recently got into a fight, was knocked to the pavement and died of an intracranial hemorrhage.

So far as diagnosis and treatment are concerned, it appears to me that these cases must be classified with those of hemorrhage from ulcer. The absence of a history of ulcer is scarcely of sufficient weight for operation to be withheld in the presence of a hemorrhage immediately threatening life, and should recovery occur under expectant treatment, further studies may be helpful in determining treatment. Such a program will result occasionally in the embarrassment of the surgeon who at operation fails to find an ulcer or other source of hemorrhage.

What he is to do under these circumstances I leave to his best judgment.

SUMMARY

A study of 337 patients admitted to the hospital because of massive hemorrhage due to peptic ulcer is presented. Of these patients 27 (8 per cent) died from hemorrhage—18 without having been subjected to operation and 9 following operations performed on 31 patients during active bleeding.

In the experience on the surgical ward service of the New York Hospital-49 (15 per cent) of all patients admitted with massive hemorrhage presented a fatal type of hemorrhage and in all probability would have died without the intervention of surgery.

Two hundred and eighty-eight patients (86 per cent) admitted because of hemorrhage recovered without immediate or early surgical intervention.

In patients with the fatal type of hemorrhage the location of the ulcer, if duodenal, is on the posterior duodenal wall and, if gastric, on the lesser curvature. The blood vessels causing the hemorrhage are the pancreaticoduodenal and the right and left gastric arteries or their major branches.

In an attempt to differentiate patients with fatal and nonfatal types of hemorrhage the most consistent criteria are failure to improve promptly under a strict regimen of bed rest, moderate doses of morphine, withholding fluids and food by mouth and adequate blood transfusions and the recurrence of hemorrhage while the patient is on a strict regimen.

If operation to save life is decided on it should be done within twenty-four or forty-eight hours of the onset of hemorrhage. The mortality in patients operated on early was 10 per cent, whereas that in patients operated on late (after forty-eight hours) was 70 per cent.

Large amounts of blood administered as transfusions before, during and after operation are of great value in operations performed for the control of hemorrhage.

Local ligation of the vessels giving rise to hemorrhage has not consistently and permanently controlled hemorrhage. Local excision of the bleeding ulcer and gastric resection, including removal of the ulcer, have given the best results.

In patients who recover from hemorrhage on a strict medical regimen the question of recommending surgery or of continuing a medical regimen is vital. No definite criteria for differentiating those who should be subjected to surgery and those who may properly be continued on a medical regimen have been developed. On the other hand, age over fifty, the occurrence of repeated hemorrhages, the chronicity and unfavorable location of the ulcer and failure in the past to respond to a medical regimen are factors suggesting surgery.

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ROENTGENOLOGIC EXAMINATION IN PATIENTS WITH BLEEDING FROM THE GASTROINTESTINAL TRACT

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MASSIVE hemorrhage from the gastrointestinal tract, particularly hematemesis, is one of the dramatic events in medicine that deeply impress both patient and physician. The question that presents itself urgently to both is, What is the cause of the bleeding? At times the history may give a clue to the diagnosis, whereas at others the bleeding takes place without any preceding symptoms or signs. In rare cases a blood dyscrasia, usually easily recognized, has prompted the hemorrhage, but the answer to the question usually depends on the demonstration of an anatomic lesion.

The roentgenologist is burdened with the responsibility of finding the source of bleeding in a patient who is often sick and difficult to examine. The plan of action which should be agreed on after thoughtful discussion by both the roentgenologist and the physician in charge of the patient, varies somewhat from case to case. If there is no clinical hint regarding the location of the point of bleeding—that is, whether it is in the upper or the lower part of the gastrointestinal tract—a scout film of the abdomen and examination of the large intestine should precede that of the esophagus, stomach and duodenum. A careful study of the small intestine forms the last part of the examination. Usually, however, the type of hemorrhage indicates roughly which part of the gastrointestinal tract is the source of bleeding, and the suspected region should be examined first. Massive hemorrhage in the majority of cases arises in the upper part of the digestive tract, and the question to be decided first is when the patient can best and safely be submitted to barium meal studies.

In the past the tendency was to delay such examination for two or more weeks, since it was thought that one at an earlier date not only endangered the patient but also, because of his precarious condition, furnished somewhat unreliable results. In recent years this attitude has changed, and the manifold advantages of early roentgenologic examination are recognized.

A patient may bleed from a gastric cancer, in which case delay of examination would mean delay in operation and, in turn, delay in removal of the malignant source of bleeding. Bleeding ulcers in people over fifty years of age have been shown to have a mortality higher than that in younger persons. The necessity of careful appraisal of these patients in whom early operation is preferable has been emphasized by Allen.¹ Should the necessity for surgical intervention arise, the operation is connected with greater risk unless the diagnosis has been established preoperatively. If the patient is bleeding from an ulcer, it is of advantage to the surgeon to know where the ulcer is—whether in the stomach or in the duodenum, and whether on the anterior or the posterior wall. The bleeding lesion may not be in the abdomen but higher in the gastrointestinal tract. A number of patients with esophageal varices have, in a search for the source of bleeding, been subjected to negative abdominal explorations. There is another reason in favor of early examination: a bleeding ulcer may heal within a short time, and examination at a later date may leave physician and patient with the uncomfortable mystery of unexplained hemorrhage.

In recent years the dietary regime of the bleeding patient has become more liberal, food being administered in the early days of hemorrhage. There is no reason to assume that a watery suspension of barium sulfate is more dangerous than food. In all probability it is even less so, because it does not stimulate peristalsis and secretion to the same degree that food does. For some time, following the example of Hampton,² I have not hesitated to examine a patient shortly after bleeding has stopped, or even during bleeding, although I do not examine patients in shock. The examination, without any palpation, is made with the patient in the horizontal position, peristalsis and gravity (turning him from side to side) being used as the means of distributing the barium over the inner surface of the esophagus, stomach and duodenum. So-called "spot films"—that is, films taken during fluoroscopy at the optimal moment of

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been a particularly discouraging one. Pathologically, the information regarding the source or sources of hemorrhage has been meager. At autopsy the pathologist has, generally speaking, failed to find an ulcer or other causes of hemorrhage. In one case the pathologist did not find even an erosion of the mucosa of the stomach and duodenum, but when the gastric artery was connected with a pressure bottle of salt solution a jet of fluid was projected from the mucosa. The area was excised, and serial sections showed a small ruptured aneurysm covered by intact mucosa. At operation in these cases the most careful inspection and palpation of the stomach and duodenum fails to demonstrate an ulcer. In some of these cases the stomach has been opened by a long incision parallel with the greater curvature, the stomach literally turned "inside out" and the entire mucosa not only of the stomach but also of the proximal duodenum carefully examined, without the demonstration of an ulcer. In the majority of cases so examined the bleeding temporarily ceased and a source of hemorrhage was not found. Yet within a week the patient may suffer another devastating hemorrhage.

Clinically patients suffering from this type of hemorrhage often fail to present any symptoms that serve to differentiate them from those with ulcer, although a clear-cut history of ulcer may be absent. The first hemorrhage may be fatal, and the assumption is that the patient has bled from an ulcer until autopsy proves otherwise. Again, patients may have repeated hemorrhages from which they recover under appropriate treatment. A patient of one of my associates whom I saw in consultation had fifty-eight massive hemorrhages over a period of twenty-five years and had been admitted to and carefully studied in many of the important clinics throughout the country. He had been operated on in one clinic and a gastric resection performed even though an ulcer was not demonstrated. He entered the New York Hospital exsanguinated from his fifty-ninth hemorrhage. He recovered and was again operated on because of the suspicion of a duodenal ulcer. A further segment of duodenum was resected, but an ulcer was not found. After having shown such a tenacity of life for so many years, it seems a pity that the patient recently got into a fight, was knocked to the pavement and died of an intracranial hemorrhage.

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In patients who recover from hemorrhage on a strict medical regimen the question of recommending surgery or of continuing a medical regimen is vital. No definite criteria for differentiating those who should be subjected to surgery and those who may properly be continued on a medical regimen have been developed. On the other hand, age over fifty, the occurrence of repeated hemorrhages, the chronicity and unfavorable location of the ulcer and failure in the past to respond to a medical regimen are factors suggesting surgery.

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to discuss them all, but a few are selected to show some of the problems with which the roentgenologist is confronted

By far the most frequent cause of bleeding is a duodenal ulcer, and good demonstration of the duodenal cap is one of the important factors in the examination. Hampton's maneuver, described above, is indispensable for this purpose, since most bleeding ulcers arise from the posterior wall and are particularly well demonstrated in this position. A normal-appearing cap does not rule out bleeding from a duodenal ulcer, since the ulcer may lie distal to the cap. Another diagnostic error may be caused by a large ulcer that replaces the entire area normally occupied by the duodenal cap and thus simulates a normal cap.

Gastric ulcers, particularly if they are not large, may disappear with unexpected speed. I have seen bleeding ulcers disappear within two weeks. As mentioned above, routine roentgenograms taken in the horizontal position may miss ulcers, particularly those high on the lesser curvature and posterior wall. Spot films, taken with the patient face up and turned on the right side, show the crater through the air of the stomach. If the ulcer lies on the posterior wall, it may be clearly seen in profile in this position.

If the bleeding is from cancer, and the cancer is large, fluoroscopy and a single spot film may be sufficient to demonstrate it. Blood clots, however, may produce a picture similar to polypoid tumor and in questionable cases should be excluded by re-examination. It should be borne in mind that a blood clot may remain unchanged in the stomach for some time, particularly if the patient has anacidity.

One of the great advantages of early examination is the possibility of diagnosing, and to a certain extent excluding, varices of the esophagus. If varices are demonstrated, in all probability the source of bleeding has been found. Varices may be present in the absence of splenomegaly, ascites and palpable liver anomalies, and hemorrhage may be the only clinical symptom. On the other hand, not every patient with demonstrable varices bleeds. The recognition of varices is difficult at times. The esophagus, if filled with enough barium, may appear practically normal except for a slight widening, or peristalsis may empty the dilated vessels, producing a normal appearance. Even when extensive varices are present, only the relief picture may reveal the vascular phenomena. The relief picture represents the barium coating of the esophagus after the main bolus has passed through it. Varices occasionally extend into the stomach, and their appearance suggests a tumor in the fundus, in rare cases they are confined to the stomach. Under these circumstances, their diagnosis is extremely difficult.

Gastritis, particularly if many erosions are present, may cause marked hemorrhage. The roent-

genologic diagnosis of gastritis is difficult and is possible in only a small number of cases. The erosive form, in which bleeding is most frequent, is rarely demonstrable, but if it is, the characteristic appearance is one of multiple shallow craters surrounded by a halo of edema. In acute alcoholic gastritis, which often causes hemorrhage, one sees evidence of marked hypersecretion with some swelling of the folds. At times this swelling produces a tumorlike appearance, but it usually disappears within a few days. On the other hand, in gastritis, the stomach may appear completely normal roentgenologically, and only by gastroscopy may the diagnosis be made.

Hemorrhage from a hiatus hernia is easily understood if a large crater is seen in the ring of the hernia, but bleeding occasionally occurs without ulcer. I have seen cases in which at autopsy nothing was found to explain the patient's hemorrhage except erosive gastritis, particularly in the herniated portion of the stomach.

Repeated hemorrhage without other clinical symptoms is often found in tumors that arise beneath the mucosa of the stomach wall — the so-called "spindle-cell tumors," which include leiomyomas, fibromas, neurofibromas and their malignant variants. Their roentgenologic appearance is similar and characteristic.

Examination of a bleeding patient should not be stopped at the duodenal cap. Tumors of the duodenum are rarer than those of the stomach, but every roentgenologist of experience has seen a fair number of them. They are frequently missed unless they are carefully looked for. Demonstration of a possible source of bleeding should not prevent one from continuing the examination to its completion unless the patient is in a precarious condition, since at times another bleeding lesion is found. I have seen, for instance, a bleeding fibrosarcoma of the third portion of the duodenum in a patient with a large duodenal crater that at first had seemed to explain the hemorrhage.

Only a few examples have been selected to demonstrate the problem with which the roentgenologist is confronted in dealing with a bleeding patient. A large number of other lesions, especially those in the small intestine and colon, have been omitted from this discussion.

SUMMARY

The roentgenologist plays an important role in the handling of a patient bleeding from the gastrointestinal tract. In most cases he is burdened with the responsibility of demonstrating the anatomic lesion that has caused the hemorrhage, and to do so it may be necessary to examine every portion of the gastrointestinal tract.

The routine roentgenologic examination of the upper gastrointestinal tract in a bleeding patient is described.

filling and projection — are taken whenever they are deemed advisable and are of great help

* * *

It may be worth while to describe the routine procedure in the roentgenologic examination of the upper gastrointestinal tract in a patient who has had a recent hemorrhage. He is placed in the supine position, rotated slightly to the left. A swallow of barium is followed through the esophagus fluoroscopically, and the presence of large varices may be detected. Further examination of the esophagus is postponed until the end of the examination, to prevent overfilling of the stomach at this stage. An additional two or three swallows are usually needed to outline the posterior part of the fundus of the stomach. Complete filling of the fundus is not obtained at this point, since it necessitates too much barium. The patient is then rotated to the right side until a point has been reached where the barium leaves the fundus and falls slowly through the body toward the antrum. More barium is given, and the stomach is observed until most of that from the fundus has emptied into the lower portion of the stomach. In this position the lesser curvature forms the dependent portion of the stomach, and ulcers may be seen clearly, face on, through the air that fills the greater portion of the body of the stomach. The significance of this position cannot be overemphasized.

The patient is then returned to the supine position and rotated slowly to the left side. This maneuver tends to produce reasonably complete filling of the upper half of the stomach. If the turning of the patient is continued until he is on his face, incomplete air demonstration of the fundus and massive filling of the lower half of the stomach result. The examination of the esophagus in both oblique diameters is completed while the patient is lying on his stomach. The examination of the duodenal cap has been described in detail by Hampton.² The outline of the cap is usually seen while the patient is in the face-down position. Better demonstration of the shape and of the relief of the cap is obtained, however, in the last phase of the examination: the patient is turned on his right side, the cap being allowed to fill with barium, after which he is returned to the supine position and to his left side. This permits the air in the stomach to reach the cap and produce an air-and-barium contrast picture of the cap (Hampton's maneuver). In the same position the antrum and second portion of the duodenum may be demonstrated with contrast filling.

Complete rotation of the patient is not always necessary, since the source of bleeding may be discovered after the first few swallows of barium or a single spot film may be sufficient for its demonstra-

tion, when the patient may return to the ward. In the patient with active hemorrhage for whom the prone position is thought to be inadvisable for clinical reasons, this part of the examination may be omitted and the patient studied only on his back and on his side, this omission will reduce somewhat the completeness of the examination.

The early examination, as described above, is adequate for study of the esophagus and satisfactory for examination of the duodenum, but it does not always demonstrate the entire stomach. The only real danger involved is in the transport of a patient bleeding from the gastrointestinal tract. I consider this danger negligible if a sudden increase in intra-abdominal pressure is prevented, and this can be avoided by lifting the patient on the bed sheet from the stretcher to the examining table and back again.

Good clinical judgment and common sense are essential in the selection of bleeding patients for early examination. Obviously a patient should not be examined during clinical shock. It is usually unnecessary to examine one while he is actively bleeding. Blood clots that lie in the stomach handicap the proper interpretation of the roentgenograms, although they do not prevent diagnosis of varices of the esophagus, large ulcers of the stomach or ulcers of the duodenum. It appears reasonable to wait at least twenty-four or forty-eight hours after an acute, massive hemorrhage. Early examination may be necessary if the patient has had previous gastrointestinal bleeding whose cause was not found, or if he shows evidence of continued arterial bleeding calling for immediate surgery. Such cases are the exception, however, and in general it is wise to postpone examination until the active, massive bleeding has subsided. If the source of hemorrhage is known from a previous examination, re-examination may be delayed until the patient's condition permits study in the upright as well as in the horizontal position. It would be useless, for example, to submit the patient and the roentgenologist to the difficulties of early examination in a case of known duodenal ulcer admitted to the hospital because of a fifth bleeding episode.

Any patient in whom early examination has not demonstrated the cause of hemorrhage should be re-examined at a later date when palpation is possible and he is permitted to stand. Some bleeding lesions are better demonstrated during the early examination, and others at the later, more convenient and more thorough one. In spite of every diagnostic maneuver known to the roentgenologist, the source of bleeding in a certain number of cases will remain obscure.

* * *

The lesions that produce hemorrhage from the gastrointestinal tract are manifold. It is impossible

throats This organism was also isolated from the throats of 3 of 21 other patients, in whom cultures were taken, for the most part toward the end of the outbreak. The first 3, with a moderate leukocytosis, as demonstrated by an average white-cell count of 12,100, were given chemotherapy. Of the 11 cases of otitis media, only 1 became purulent and required chemotherapy. White-cell counts

or the Lee strain of influenza B, the procedure has been described elsewhere in detail.¹ In Group 1 the average final titer, determined as the reciprocal of the final dilution of serum before the addition of sensitized cells, was definitely elevated against influenza A — 1:421, or over twice as high as the titer of 1:192 (1:64 in the initial dilution of serum) regarded by Eaton and Rickard² as presumptive

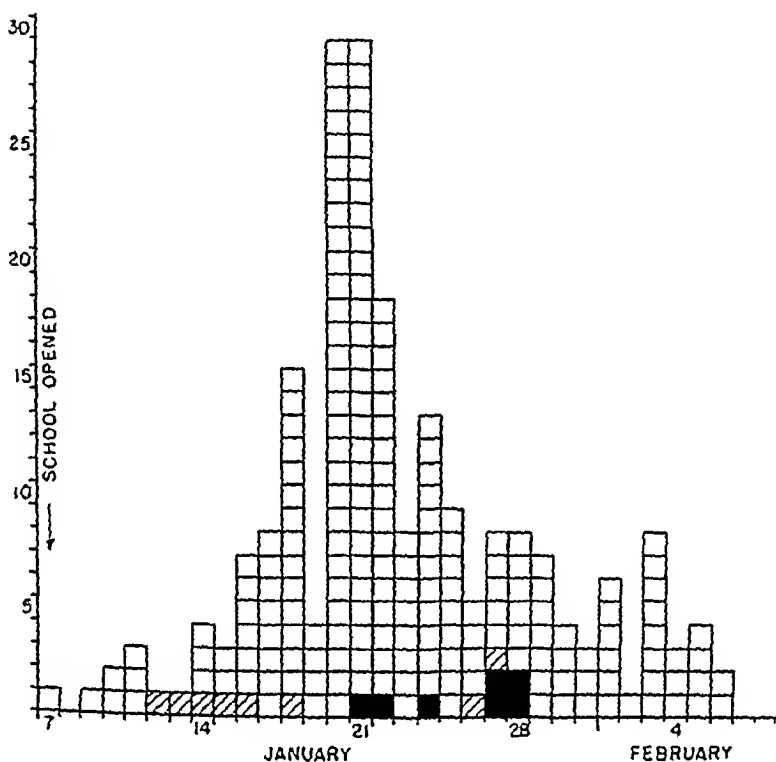


FIGURE 1 Incidence of Cases

The empty squares represent case admitted because of upper respiratory infection, the cross-hatched squares, those tested for complement-fixing antibodies during the convalescent stage, and the black squares, those tested for complement-fixing antibodies during the acute and convalescent stages

taken in 6 of these cases ranged between 7800 and 23,200, averaging 16,500. The 3 cases of pneumonia were clinically similar to so-called "primary atypical pneumonia of unknown etiology," but the patients had relatively high initial white-cell counts (average 18,500) that remained elevated for several days and then responded to penicillin.

Serologic studies were made in 8 cases during the convalescent stage, twelve to seventeen days after the onset of symptoms (Group 1), and in 7 others during both the acute, that is, the first three days, and convalescent stages (Group 2). Patients in the former group are indicated in Figure 1 by cross-hatched squares, and those in the latter by black squares.

Complement-fixation tests were carried out with the use of the allantoic fluids from embryonated eggs infected with the PR8 strain of influenza A

evidence of recent infection. Furthermore, 7 of the 8 patients tested showed titers of 1:192 or higher. The average titer against influenza B was 1:57, and in 1 case the titer was elevated, being 1:384.

In Group 2 the average titer against influenza A was approximately ten times as high in serums taken in the convalescent phase of the infection as in those taken in the acute phase, — 1:495 in the former and 1:42 in the latter, — and in 5 cases the titer increased fourfold or more following recovery. The average titer against influenza B was 1:90 in the convalescent and 1:09 in the acute phase. In only 1 case was there an increase in antibody reaction to influenza B, and in this case the titer during convalescence was relatively low, making the interpretation of the test uncertain.

Indications and contraindications for roentgenologic examination soon after, or during, hemorrhage are discussed

In spite of the most careful examination, the cause of bleeding may remain roentgenologically obscure

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AN OUTBREAK OF INFLUENZA A IN A BOYS' SCHOOL*

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FOLLOWING the Christmas vacation of 1945-1946, there were admitted to the infirmary of a boys' school of about 680 boarding students, located thirty miles north of Boston, several boys with "colds" characterized by enough malaise so that the patients willingly sought medical advice. After hospitalization of the first patient 30 patients were admitted for upper respiratory infections during the next ten days, 138 more during the second ten-day period and 46 more during the third ten days. The outbreak then subsided. The epidemiologic data are presented graphically in Figure 1.

CLINICAL ASPECTS

These illnesses of the respiratory tract were diagnosed clinically as common cold in 87 cases, influenza in 97, acute pharyngitis in 14, otitis media in 11, hemolytic streptococcus pharyngitis in 3 and primary atypical pneumonia of unknown etiology in 3.

Detailed questioning of 50 patients selected at random disclosed that the onset of symptoms was gradual in 46 and abrupt in 54 per cent. Constitutional symptoms included malaise in all cases, headache in 68 per cent, chilliness in 44 per cent and muscle aches in 26 per cent. Cough was noted in all cases, coryza and a sore or "scratchy" throat in 68 per cent and earache in 32 per cent.

In about 80 per cent of the cases the first symptom was one referable to the upper respiratory tract, such as a sore or "scratchy" throat, "stiffness," "sniffles" or a "cold" or cough. In the remaining 20 per cent the first symptom was malaise or prostration.

The symptom of malaise is more difficult to define than it is to experience. The statement that malaise was present in all cases means that all the 50 patients questioned minutely felt "lousy" at approximately the time they sought hospitalization. This word usually chosen by the patient, although

of doubtful elegance, has the merit of being unmistakable in its connotation of lack of well being. A more accurate picture of the systemic symptoms is afforded by the fact that whereas all the boys interrogated had at least transient malaise, only 21 per cent of the whole group had abnormal fatigue and weakness — that is, prostration — as evidenced by remarks made on the infirmary records.

Likewise the fact that all those closely questioned had cough needs some qualification. In many cases the reply to the question, "Did you have a cough at any time?" was, "Well, not enough to speak about." Further interrogation, however, elicited the information that such a patient had a slight "hack" or a "scratchy cough." Cough was thus present to a greater or less degree in each member of this group but was noticeable enough to be recorded in the infirmary records in only 20 per cent of the total number of patients.

PHYSICAL AND LABORATORY FINDINGS

As one might suspect, objective signs were scant except for injection of the mucous membranes of the nasopharynx or the tympanum and for a variable amount of coryzal discharge.

The average temperature was 101°F at the height of the illnesses, — usually at or shortly after admission, — the range being between 98 and 104°F. There was nothing distinctive about the charts, which showed, in general, a fairly rapid return to normal recordings during the first day or two of hospitalization.

White-cell counts revealed a definite although slight leukopenia on the average. In 25 cases with all the clinical signs of influenza, the white-cell count ranged between 2600 and 9600, with an average of 5500. In the serologically studied group, counts in 6 cases ranged between 4100 and 8600, averaging 5800, on admission. In 1 case a white-cell count of 7600 on admission was found to be 4800 during the height of the illness, with a return to 8300 before discharge.

During the outbreak, there were remarkably few clinical complications. Three patients were diagnosed as having a hemolytic streptococcus pharyngitis, the organism having been cultured from their

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RADIATION TREATMENT OF LOCALIZED MALIGNANT LYMPHOMA*

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THE term "malignant lymphoma" has been rather generally accepted, in America at least, to designate malignant tumors that are characterized by progressive enlargement of lymphoid tissue in various parts of the body. Pathologists have subdivided this group on a histologic basis into several more or less characteristic types. Clinically, the disease as a rule progresses with a varying degree of rapidity to a fatal termination, the average duration of life being from two to three years.¹ Gall and Mallory² reported 10 cases with survival, free of disease, for six years or more after surgical removal. In a more recent paper, Gall³ added to the number. Jackson and Parker⁴ report survivals up to twenty-four years, and others¹ claim fairly long survival rates.

That a certain number of patients with malignant lymphoma have been cured of their disease there can be no doubt. What are the factors responsible for these unexpected, favorable results, and can the same results be obtained with properly applied irradiation as with surgical procedures? It is with these questions that the present paper is concerned.

As in other types of malignant tumors, cure in malignant lymphoma may be assumed to depend on the extent of the disease at the time treatment was undertaken, as well as on the histology, the location of the tumor and the effectiveness of the treatment. Experience has shown that widely disseminated malignant tumors are not curable by any method of treatment at present available. Cure seems to depend on complete removal or destruction of the primary tumor before it has had an opportunity to spread beyond its immediate site.

Is there a time in the life history of a malignant lymphoma when it, like other forms of malignant tumors, may be considered a localized disease? Recent opinion seems to favor an affirmative answer to this question. Gall reports a patient who died of intercurrent disease four and a half years after the successful surgical removal of a follicular lymphoma of the inguinal lymph nodes. Autopsy failed to show any evidence of lymphoma. Further confirmation of this assumption is obtainable from a review of all patients who have survived, free of disease, for long periods. In nearly all such cases a localized lesion was present when treatment was undertaken.

On the supposition that the preceding hypothesis is correct, we have reviewed the records of approximately 500 patients with malignant lymphoma treated at the Massachusetts General and the

Collis P. Huntington Memorial hospitals, and selected for particular study only those who were alive and apparently free of disease five years or longer in whom the lesion at the time of treatment was localized and who were treated with irradiation only, biopsy excepted. We have attempted to determine whether the favorable results in this group were due to the type of the lesion, the location of the lesion or the method of treatment, or whether no explanation could be obtained.

Histologic Classification

If the leukemias and the paraganuloma of Jackson and Parker⁴ are excluded, two classifications are generally accepted in this community — that of Gall and Mallory² and that of Jackson and Parker.⁴ The classifications are as follows:

GALL AND MALLORY	JACKSON AND PARKER
Stem-cell lymphoma	Reticulum-cell sarcoma
Clasmatoctytic lymphoma	
Lymphoblastic lymphoma	Lymphosarcoma
Lymphocytic lymphoma	
Hodgkin's lymphoma	Hodgkin's granuloma
Hodgkin's sarcoma	Hodgkin's sarcoma
Follicular lymphoma	Giant follicular lymphoma

It will be noted that, except for slight differences in nomenclature, there is no marked divergence in classification.

Material

We have been able to collect 15 cases in which the histories conform with the problem as outlined — a single lesion at the time of treatment (which consisted primarily of radiation), diagnosis established by biopsy and the patient living and free of disease more than five years after the last course of treatment. Table 1 gives the pertinent data on this group of patients. Five were males, and 10 were females. The youngest was ten, and the oldest fifty-eight years old, the average age being thirty-seven years. The location of the lesion varied. There were abdominal tumors, either in the mesenteric lymph nodes or in some part of the gastrointestinal tract, in 4 cases. The tumor was in the peripheral lymph nodes in 5 cases, the involved nodes being in the neck in 4 and in the groin in 1. The remaining tumors were in the tonsil in 2 cases, the larynx in 1, the parotid gland in 1, the femur in 1 and the skin in 1.

Histologically, there were 2 stem-cell, 1 clasmatoctytic, 6 lymphoblastic, 3 lymphocytic and 1 Hodgkin's lymphoma, 1 Hodgkin's sarcoma and 1 follicular lymphoma.[§]

§Slides of all these tumors were reviewed microscopically in 1946 in the Department of Pathology, Massachusetts General Hospital.

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DISCUSSION

The results of the complement-fixation tests in Group 1 alone afford presumptive evidence for regarding the outbreak as predominantly due to influenza A. With one exception, no titer as high as 1:192 was obtained for influenza B. Although infections caused by influenza B had been prevalent in the eastern United States about two months previously, with this one exception, only extremely low concentrations of antibody, or none at all, were demonstrated. More conclusive serologic evidence that the outbreak was due to influenza A is afforded by the results of the tests on the 7 patients in Group 2.

Since an etiologic diagnosis of influenzal infection is at best equivocal on clinical criteria alone, it is of interest to compare clinical diagnoses in the serologically proved cases with those made during the course of the whole outbreak (Table 1). Although

TABLE 1 Diagnoses in All and in Serologically Positive Cases

DIAGNOSIS	ALL CASES		SEROLOGICALLY POSITIVE CASES	
	NO OF CASES	PER-CENTAGE	NO OF CASES	PER-CENTAGE
Otitis media	11	5	1	7
Common cold	87	40	5	33
Influenza	97	45	9	60

the number of serologically tested patients was small, it represented a rough cross section of the outbreak. Accordingly, the variations in clinical diagnosis appeared to reflect for the most part variations in the symptomatology rather than in the etiology of the disease.

It will be observed that during the outbreak, almost as many common colds were diagnosed as were cases of influenza. Of the 50 boys carefully questioned, 28 per cent regarded themselves as merely suffering from a cold and as doing the sensible thing by reporting to the infirmary. That this commendable attitude was not altogether a lofty application of principles of preventive medicine is suggested by the fact that four times as many boys reported on Sundays—usually in the late afternoon—and Mondays as on Saturdays. (The numbers reporting on different days of the week, beginning Saturday, were 11, 46, 45, 32, 22, 26 and 33.) The questionnaire was directed only to the hospitalized group, however, and it is evident that any infected boy who did not feel sick enough to report to the infirmary, if he had any symptoms at all, regarded himself as merely suffering from a cold. One of the three authors had a cold during the

outbreak, but was able to continue working, another had influenza, requiring him to go to bed for a few days.

Although this work is in no sense meant to be construed as a study of "colds," it is pertinent to stress the fact that almost half the patients, as diagnosed by both medical and lay criteria, had common colds. These findings serve to emphasize earlier observations that clinical symptoms of different types of respiratory infections may overlap so much that the clinical differentiation is generally unreliable.* It is apparent that a cold may be both a symptom and a sign, and that even the diagnosis "common cold" is symptomatic rather than etiologic.

Finally, it is of interest, in view of our findings, to refer to the epidemiologic prediction of the Fort Bragg Commission on Acute Respiratory Diseases⁴ based on observations of the cyclic character of influenza outbreaks. The commission stated that the probabilities were seven out of eleven that influenza A would reappear during the winter of 1945-1946. This reappearance of influenza A in what up to midwinter had been an influenza B year is all the more interesting in that the "present theory" of the commission also called "for a widespread epidemic [of influenza B] before the summer of 1946."

SUMMARY

An epidemiologic and clinical description of upper respiratory infections occurring in a boys' boarding school in January and February, 1946, is given.

Complement-fixation tests were made for influenza A and B on the serums of 8 boys during convalescence and of 7 others during both the acute and convalescence phases. The average titer against influenza A among the convalescent patients was found to be more than double that considered presumptive evidence of recent infection. When the seven paired serums were tested, the average titer during the convalescent phase was found to be approximately ten times as high as that during the acute phase.

On the basis of the serologic evidence in this outbreak, the virus of influenza A appeared to be the predominant etiologic agent.

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if the destruction of the tumor is complete. The radiation dosage should be large enough to accomplish this. In some cases the dosage may be as little as 600 r, but as a rule it is wiser to give as much as the normal tissues will tolerate without undue damage. With supervoltage (1200 kilovolts) and heavy filtration, the dosage may be as high as 2000 r.

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MEDICAL PROGRESS

BIOCHEMICAL ABNORMALITIES DURING RENAL INSUFFICIENCY (Concluded)*

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Calcium and Phosphorus

Calcium and phosphorus are predominantly localized in bone, but both elements occur in the cell,⁸ phosphorus being particularly important. Inorganic phosphate is the chief anion in the intracellular fluid, and the organic phosphates of the cell appear to have considerable significance in the metabolism of fats and carbohydrates, the energetics of cellular activity and the physiology of muscular contraction. The extracellular water content of calcium and phosphorus is small in absolute amounts, but it is vital in the maintenance of normal neuromuscular irritability and bone structure. In addition, both substances play a role in acid-base regulation of body fluids. As with the other electrolytes, both ions are constantly undergoing exchange and exist in dynamic equilibria.^{74, 75}

Calcium exists in the plasma in two forms — one completely ionized and highly diffusible, and the other bound to protein and indiffusible. A small proportion is also indiffusible because it is linked to phosphate and citrate in colloidal aggregates.⁸ The inorganic phosphate of the plasma diffuses readily through colloid membranes and is apparently not bound to protein.^{4, 76} About half the phosphorus in the plasma is incorporated in the molecules of various lipids and fatty acids that may participate in base binding.⁷⁷

The plasma concentrations of ionic calcium and phosphate are resultants of the interaction of many factors. Chief among these are the relative concentrations of protein, hydrogen and bicarbonate ions. Moreover, calcium and phosphate levels tend to vary reciprocally under most circumstances for reasons that are not understood. It is now well established that the secretion of the parathyroid

glands, parathormone, is influential in controlling the concentrations of both ions.⁷⁸ The manner in which parathormone accomplishes this is a matter of controversy. On the one hand, it is believed that parathormone reduces the phosphate concentration by decreasing its renal tubular reabsorption,^{79, 80} the subsequent hypophosphatemia inducing hypercalcemia and mobilization of fixed calcium physicochemically, and on the other, that parathormone acts directly on the bone to mobilize calcium.^{81, 82} There is evidence that both actions may occur.⁸³ Finally, normal calcium-phosphorus metabolism depends on adequate dietary intake and intestinal absorption. Vitamin D is essential to the latter.

Both calcium and phosphorus are important constituents of the glomerular filtrate. During the passage through the tubules, both are reabsorbed by separate mechanisms and conserved or discarded in accordance with the needs of the body and the demands of the various processes in which they participate.

Relatively little is known about the mechanism of tubular calcium reabsorption. The calcium in the glomerular filtrate, which is limited to the ionized fraction, apparently undergoes extensive reabsorption.⁴ Hypercalciuria results when calcium is injected intravenously⁸⁴ and during hypercalcemia in hyperparathyroidism.⁸⁵ These findings suggest that the reabsorptive mechanism can be saturated, but this possibility has never been examined quantitatively.

Convincing quantitative evidence that phosphate is removed from tubular urine by a mechanism of limited capacity is now available.⁷⁶ At high plasma levels of phosphate, the rate of reabsorption becomes constant and excess phosphate is lost in the urine. This maximal activity is inhibited by glucose reabsorption. Nevertheless, an independent mechanism is apparently involved since phlorrhization enhances phosphate reabsorption whereas it halts

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The x-ray dosage given was 1000 r or less in 9 cases, between 1000 r and 2000 r in 4 and over 2000 r in 2, extensive radium treatment was given in 1 case

Analysis of Factors

Location The location of the tumor does not seem to be the predominant factor on which survival can be based, but it is of some importance. In 4, or about a third, of the patients the lesion was in the abdomen. This percentage is quite comparable to that

confirm this supposition, but the number of cases is too small to warrant a positive statement.

Extent of lesion No long survivals, apparently free of disease, occurred in patients with multiple lesions. Localization of the disease at the time treatment is undertaken is probably an essential factor for lasting cure.

Method of treatment The work of Gall and Malory appears to show that complete surgical removal may produce permanent cure, and our findings in-

TABLE 1 Data in Patients Apparently Free of Disease More Than Five Years after Treatment

AGE yr	SEX	PATHOLOGICAL DIAGNOSIS	LOCATION OF TUMOR	ONSET OF DISEASE	TREATMENT AND DOSAGE	FIRST TREATMENT	LAST TREATMENT	LAST EXAMINATION	SURVIVAL	
									SINCE ONSET yr	SINCE TREATMENT yr
55	F	Stem cell lymphoma	Ileum	Oct., 1939	Radium (++++)	Nov, 1939	Feb. 1940	Dec., 1945	6 2/12	5 10/12
25	M	Stem-cell lymphoma	Cervical lymph nodes	June 1932	X-ray (1200 r)	June 1932	Dec. 1932	Dec., 1945	13 6/12	13
17	F	Clasmatoctytic lymphoma	Femur	Dec., 1935	X-ray (3000 r)	Aug. 1936	Aug. 1936	July 1946	10 6/12	9 10/12
10	F	Lymphoblastic lymphoma	Cervical lymph nodes	Mar., 1932	X ray (400 and 800 r)	Apr., 1936	Apr. 1940	Dec., 1945	13 9/12	5 8/12
44	F	Lymphoblastic lymphoma	Mesenteric lymph nodes	Oct., 1939	X ray (1200 r)	Jan., 1940	Mar., 1940	Mar., 1946	6 5/12	6
41	F	Lymphoblastic lymphoma	Larynx	Oct., 1932	Radon seeds (10) X ray (900 r)	Apr., 1933	Apr. 1933	Apr., 1946	13 6/12	13
57	F	Lymphoblastic lymphoma	Skin	June, 1934	X ray (900 r)	Aug. 1934	Sept. 1934	July, 1944	10 1/12	9 10/12
58	F	Lymphoblastic lymphoma	Tonsil	Apr., 1937	X ray (3000 r)	May, 1938	Apr., 1940	Mar., 1946	8 11/12	5 11/12
12	M	Lymphoblastic lymphoma	Cervical lymph nodes	Dec., 1916	Radium (++++)	July 1918	Dec. 1920	May, 1946	29 5/12	25 5/12
37	F	Lymphocytic lymphoma	Parotid gland	Jan., 1938	X ray (600 r)	Nov., 1938	Dec. 1938	Nov., 1945	7 10/12	6 11/12
45	F	Lymphocytic lymphoma	Tonsil	Jan., 1938	X ray (1500 r)	Feb., 1938	Jan., 1940	Feb., 1946	8 1/12	6 1/12
35	F	Lymphocytic lymphoma	Cervical lymph nodes	Aug., 1934	X ray (900 r)	Sept., 1934	Sept., 1934	Oct., 1945	11 2/12	11 1/12
35	M	Hodgkin's lymphoma	Mesenteric lymph nodes	— 1926	X ray (300 ma min and 400 and 800 r) erythema dose)	Apr. 1930	Jan. 1931	Mar., 1946	20	15 2/12
45	M	Hodgkin's sarcoma	Retroperitoneal lymph nodes	Oct. 1928	X-ray (300 ma min and 400 and 800 r)	Apr. 1930	May 1936	Jan. 1946	17 3/12	9 8/12
22	M	Follicular lymphoma	Inguinal lymph nodes	Jan., 1937	X ray (600 r)	Mar., 1937	Mar., 1937	Aug. 1945	8 7/12	8 5/12

found by Gall. In another 5 cases, the lesion was in the peripheral lymph nodes, and in the remainder, in various other locations. Among students of this disease, there is a general opinion that when malignant lymphoma is localized, particularly in the gastrointestinal tract — or in the long bones⁵ — and can be completely removed, a cure may be expected in a fair percentage of cases. Our findings may be interpreted as confirming this belief. Otherwise, the location of the single lymphomatous tumor seems to be unimportant.

Histology It is known that the duration of life in a given case is somewhat dependent on the type of tumor present, and one would expect the chance of permanent cure to be best in the slowly growing, less malignant tumors. The data presented do not

indicate that the same results may be obtained by irradiation, provided the dose is sufficient to destroy the tumor. The minimum dose that will produce this result is not known, and our data do not give additional information. The smallest dose given was 600 r, and the largest 3000 r. Some of the tumors must have been extremely radiosensitive and others quite resistant, unless it is to be assumed that in some cases recovery was spontaneous.

CONCLUSIONS

Localization of the disease in malignant lymphoma, as in other malignant tumors, is a most important factor in suggesting a favorable prognosis. Apparent clinical cure or remission may be obtained by irradiation as well as by surgical removal.

ported cases among Northern Chinese that appear to resemble those usually described as renal rickets in which the plasma phosphate concentration remained low. All these conditions, and possibly some others, must be considered apart from the more frequent syndrome of hypocalcemia, hyperphosphatemia and acidosis that leads to bony distortions during protracted renal insufficiency.

In the controversy regarding renal rickets, it is evident that several areas of disagreement may be defined. In the first place, it appears that the name "renal rickets" may be misapplied, since most pathological studies have revealed that the bone lesion is identical with that produced by hyperparathyroidism — generalized osteitis fibrosa^{95, 105}. It is agreed that the failure of epiphyseal closure seen on x-ray examination denotes a rachitic alteration, but on the whole the roentgenographic findings are not helpful in reaching a decision. Earlier workers¹⁰⁵ considered the bone lesion similar to that of rickets, but their descriptions tally, for the most part, with the pathological picture of osteitis fibrosa. Recently, Folis and Jackson¹⁰⁷ found microscopic changes in the bone in 19 of 39 cases of chronic renal insufficiency in adults, in most of which it appeared that broadening of the osteoid sheaths of the bone trabeculae and increased bone destruction, with replacement by fibrous tissue, occurred simultaneously. They interpreted these changes as evidence of coexistent osteomalacia and osteitis fibrosa, and claimed that osteomalacic alterations were predominant. These conclusions are in disagreement with those of Ginzler and Jaffe¹⁰⁵ in a similar series and await confirmation. In general, the mass of evidence favors the view that osteitis fibrosa is the typical lesion.

The discovery of parathyroid hyperplasia, together with the demonstration of osteitis fibrosa, in many of these cases, has elicited enthusiastic claims that the condition should rightfully be called "renal hyperparathyroidism" and that excess production of parathormone is responsible for the bone lesions^{105, 109}. The weight of the evidence now available in the literature appears definitely to favor the view that parathyroid hormone may cause decalcification of bone in experimental animals after bilateral nephrectomy,⁹⁵ but it is also clear that the development of acidosis contributes heavily to the process of bone resorption. Hence, it is possible that parathormone is active in chronic renal insufficiency, but it cannot be accounted the chief cause of bone change. Since it has been pointed out that the histology of secondary parathyroid hyperplasia differs strikingly from that of primary disease,⁹⁶ it is possible that parathormone production in man is in no way comparable to the dosage administered nephrectomized rats, as described by Ingalls et al.⁹⁵ The causes for secondary hyperplasia remain obscure, attention having been

paid to hypocalcemia,⁹⁵ hyperphosphatemia,¹¹⁰ total calcium-phosphorus imbalance¹⁰⁵ and acidosis.⁹⁵ It has been suggested that the hypertrophy represents compensation rather than overactivity, in response to the need for maintaining the ionic calcium content of plasma.⁹⁵

Since acidosis is always present and since acidosis and a low-calcium diet have been found to produce osteitis fibrosa in experimental animals,¹¹¹ it seems not unlikely that chronic acidosis may be at the root of the disorder. This factor would be expected to result in mobilization of calcium from the bones and, in the presence of renal insufficiency, in a reduction of the absorption of calcium from the bowel. Ginzler and Jaffe¹⁰⁵ suggest that periods of fluctuation of renal insufficiency and acidosis with new-bone deposition, followed by further resorption, may be expected to produce the degree of osteosclerosis they observed in their series. In line with the view that insufficient calcium absorption occurs are the findings that vitamin D administration occasionally results in improvement⁹⁵ and that the fecal loss of calcium is too small to arise from excessive withdrawal from bone.⁹⁵ It seems more probable that a persistent reduction of calcium absorption is operative.

A somewhat different type of osseous abnormality, compatible with normal growth, has been described in nephrotic children. Emerson and Beckman¹¹² have consistently found hypocalcemia, mainly attributable to a deficiency of the protein-bound fraction, in these patients associated with rarefaction of the diaphyses of bone. No abnormality of epiphyseal calcification was noted, however. For some reason, calcium uptake from the bowel was markedly reduced and renal excretion of calcium fell, apparently as a result of the need for calcium conservation. This metabolic abnormality has been described in other cases.¹¹³ The changes often cleared during remissions of the disease, when the plasma protein concentration returned toward normal.

Other Electrolytes

So far as their relative plasma concentrations are concerned, the remaining electrolytes of the body fluids are unimportant. Moreover, so far as knowledge goes, it appears that these substances acquire little added significance during renal insufficiency, although it must be admitted that the information at hand is unsatisfactory, since these substances are difficult to determine.

Sulfate retention is known to occur^{114, 115} and probably contributes to acidosis. This ion is excreted efficiently by the kidney, undergoing little reabsorption during its passage through the tubules.¹¹⁶ It is interesting that sodium chloride excretion is depressed when sulfate ions are present in excess, and it is possible that this is a contributing factor in certain cases of salt retention. Sulfate

that of glucose. Parathormone is also considered to reduce phosphate reabsorption.⁸⁶ The phosphate salts in the urine play a significant role in the excretion of hydrogen ion, as pointed out above, but it now appears that acid-base imbalance has no influence on their tubular reabsorption.⁷⁶ It seems possible to explain claims to the contrary⁸⁷ on the basis of changes in the quantity of phosphate available for excretion rather than on the basis of renal functional alteration.

In renal insufficiency the reduction of filtration depresses the renal excretion of both phosphate and calcium. It is a curious, and thus far inexplicable, fact that only phosphate is retained, as a rule, in this situation. The retention of phosphate leads to depression of the calcium ion level and increased loss of calcium in the feces. The preferential retention of phosphorus may be accounted for on the basis of dietary imbalance, since the diet usually contains somewhat more phosphorus than calcium.⁸ The renal excretion of calcium and phosphorus generally parallels the intake, but with loss of renal control it is possible that phosphorus accumulates more rapidly than calcium and thus sets in motion other reactions that produce hypocalcemia. This point of view is supported by the fact that low-phosphorus diets⁸⁸ or increased fecal excretion of phosphorus following the ingestion of precipitating agents, such as aluminum hydroxide,⁸⁹ may correct the calcium-phosphorus imbalance during uremia. The recent demonstration of phosphate mobilization during stress^{90, 91} provides another possible explanation of hyperphosphatemia in uremia.

Hypocalcemia can develop, however, in the absence of phosphate retention, apparently as a result of impaired intestinal absorption.^{85, 92} Since vitamin D does not wholly correct this defect, it has been suggested that inactivation of the vitamin may occur.

Tetany due to a diminished plasma concentration of calcium ions is a frequent feature of uremia. As a rule, its manifestations are mild, consisting of muscle cramps and twitching and hyperirritability of motor nerves. Occasionally, however, convulsive seizures occur. Mason and his co-workers⁹³ have found that tetany and convulsions follow the reduction of calcium ion concentration in the cerebrospinal fluid rather than in the plasma.

Bony abnormalities may develop in renal insufficiency of long duration associated with chronic acidosis. Growing children in particular may present striking changes resembling rickets, often with serious deformities due to maldevelopment, epiphyseal separation and pathologic fractures. Adults seldom suffer from a severe grade of skeletal involvement, but histologic alterations may be found in most cases. In addition, so-called "metastatic calcification" may occur. Mönckeberg's medial sclerosis or diffuse calcification may involve the

arteries, and calcium plaques may appear in the subcutaneous tissues.^{94, 95}

Medical writings on these subjects are conflicting and confused, little agreement has been reached regarding either the cause or the character of skeletal changes. This controversy is evident in numerous descriptive terms that include "renal rickets," "renal osteomalacia," "renal dwarfism," "renal hyperparathyroidism," "renal osteodystrophy" and "renal osteitis fibrosa."

It is generally agreed that protracted renal insufficiency, chronic acidosis, low plasma calcium concentration and phosphate retention are common to most of these cases. Moreover, parathyroid hypertrophy has been found in most cases when a careful search has been made at autopsy.⁹⁶ Regarding the character of the bone changes and their causation, however, opinion is sharply divided.

The difficulty of interpreting the physiology of certain other skeletal disorders that result in or apparently arise from renal dysfunction complicates the dispute still more. Hyperparathyroidism, caused either by parathyroid adenoma or by idiopathic diffuse hyperplasia of the parathyroid glands, may produce marked renal damage. The increased secretion of parathyroid hormone leads to increased renal phosphate excretion and, in turn, to hypophosphatemia, hypercalcemia and finally hypercalciuria.⁹⁷ Calcification of the kidney tubules, the formation of calcium stones and the subsequent complication of pyelonephritis lead, in many cases, to fatal uremia.⁹⁸ Cystine-storage disease⁹⁹ likewise causes renal damage and bony abnormalities somewhat similar to those of rickets. Few cases have been reported, and nothing is known of the biochemical alterations. Cystine deposits and cystine calculi have been found in the kidneys. In contrast to these metabolic and endocrine disturbances are certain rare conditions in which anomalies of renal function lead to biochemical and skeletal defects that are different in some respects from those frequently seen in renal insufficiency. A few cases of renal glycosuria, hypochloremia, hypophosphatemia, hypocalcemia and acidosis, usually associated with dwarfism, have been reported.^{100, 101} McCune, Mason and Clarke¹⁰⁰ suggest that this so-called "Fanconi syndrome" results from a developmental defect of the renal tubules that permits loss of glucose, phosphate and base. The chronic acidosis is considered to be the cause of the skeletal deformity. A somewhat similar disorder described in adults as well as in children,¹⁰²⁻¹⁰⁴ in which renal damage appears to be secondary to deposits of calcium in the kidney, differs from the Fanconi syndrome in presenting hyperchloremia and in the absence of glycosuria. Albright and his associates¹⁰² suggest that the primary defect is a tubular inability to secrete an acid urine, calcium taking the place of deficient base in the urine. Snapper⁹⁵ and others⁹² have re-

and during shock, cannot be prevented by dietary measures¹²⁷ and is apparently not attributable to tissue destruction or disuse atrophy.¹²⁵ It has been suggested¹²³ that this phenomenon is related to Selye's¹²³ "alarm reaction" and may possibly be due to excess secretion of the so-called "S hormone" by the adrenal cortex. It is entirely possible that similar factors are operative in some cases of renal insufficiency and account, in part, for azotemia. Certainly, the characteristic wasting is attended by mobilization of nitrogen and negative nitrogen balances have been observed in chronic renal disease.¹²⁹ From a therapeutic standpoint, it is interesting that desoxycorticosterone appears to retard the elevation of nonprotein nitrogen in nephrectomized rats.⁷³

Urea

Urea mounts in the blood following a reduction of glomerular filtration rate more rapidly than other nitrogenous substances and makes up an increasingly larger fraction of the nonprotein nitrogen. Tubular reabsorption of urea appears to be passive, increasing as the urine flow falls.¹³¹ It is not surprising, therefore, that urea retention should be prominent when filtration reduction is only moderate, since the slowing of the stream of glomerular filtrate permits a larger fraction of the urea to return to the blood by diffusion. An adequate correlation between the filtration rate and the plasma urea concentration, however, does not obtain throughout the course of renal disease.¹³¹ Indeed, the urea level may remain essentially normal until renal insufficiency is marked. This behavior apparently depends on several factors. Tubular diuresis may decrease urea reabsorption and counteract in a small way the effect of defective filtration. But it seems likely that decreased ingestion of protein, as a result of anorexia, is more important in preventing elevation of plasma urea. Moreover, it is possible that urea production is diminished.¹³²

It has been proved that urea is relatively non-toxic in the concentrations usually found in uremia.¹³³ Indeed, patients with blood urea nitrogen concentrations persistently above 200 mg per 100 cc may pursue active lives for several years. It has been suggested, however, that urea interferes with detoxification in the body and permits the accumulation of more toxic substances.¹³²

Creatinine and Guanidine

Creatinine, like urea, appears to be an end product of metabolism that lies outside the metabolic pool.³ These compounds cannot be used by the cells in any manner and must be removed from the body as they accumulate. The addition of creatinine to the blood, however, is relatively slow, and its plasma level does not rise proportionately as high as that of urea.¹³⁴ Hence, creatinine retention tends to occur only after renal disease is far

advanced and is therefore considered to have greater prognostic significance than urea. This phenomenon is possibly based, in part, on the fact that in man creatinine is excreted by tubular activity as well as by filtration.¹³⁵

Guanidine, a highly toxic compound related to creatinine, has aroused considerable interest because of studies indicating an increase of this substance in the blood during uremia that parallels the development of the symptoms.^{93, 137, 138} But it does not follow that this relation is causal, nor has it been proved that the blood guanidine even reaches a toxic level, since the methods of determining it are unsatisfactory and relatively nonspecific.

Uric Acid

The degradation of nucleoproteins in man ends in the production of uric acid, which is excreted in the urine after filtration through the glomerulus and partial reabsorption by the tubules. The details of the metabolism of this curious substance remain unsolved. It possesses unusual physiochemical properties that give it value in water conservation among reptiles and birds,⁴ but that are apparently of little benefit to man. In gout, deposits of the material in synovia and cartilage are associated with abnormalities of its excretion, hyperuricemia and arthropathy. Likewise, uric acid accumulates in the plasma during renal insufficiency, but whether this circumstance is responsible for goutlike episodes of synovitis, bursitis and arthritis is unknown.

It has been claimed that uric acid is retained in the blood during renal insufficiency earlier than any other substance and that such retention has considerable value from the diagnostic viewpoint.^{134, 135} This claim has been disputed,¹³⁹ but it appears to be true for many cases. It is of great interest that hyperuricemia may be one of the earliest evidences of pre-eclampsia.¹⁴⁰ Chesley and Williams¹⁴¹ have found that this phenomenon is caused by a reduction of uric acid clearance secondary to a decrease in the glomerular filtration rate and an increase in tubular reabsorption rather than by a change in metabolism, as others have claimed.¹⁴⁰

Glucose

Glucose is typical of the second group of substances discussed above. It is reabsorbed from the glomerular filtrate almost completely. This process of conservation is rarely disturbed even in advanced renal disease when water and salt are lost in abundance. Rarely, renal glycosuria does occur, but for the most part the reduction in filtration rate appears to outstrip the reduction in tubular activity so that the capacity for glucose reabsorption is not exceeded. A disturbance of carbohydrate metabolism, however, has been demonstrated by Linder, Hiller and Van Slyke.¹⁴² In far-advanced renal disease, an abnormal blood sugar curve was found following the ingestion of glucose. The glucose con-

is retained early in the course of renal insufficiency and has been suggested as a more reliable index of renal failure than the concentration of most other substances¹¹⁴

Magnesium, likewise, often accumulates in the blood during renal insufficiency, but it appears that the concentrations attained are never sufficiently high to evoke symptoms on the basis of its own pharmacologic activity¹¹⁷⁻¹¹⁹

NONELECTROLYTES

Most of the solid matter in solution or in colloidal suspension in the plasma is organic and nonelectrolytic in nature. These substances vary widely in complexity from the small molecule of urea to the highly intricate structures of the various plasma proteins and fats. In general, they comprise what has been termed the "metabolic pool," existing in equilibrium, like the electrolytes, with similar substances within the cells and readily available for use in various intracellular reactions. Certain substances, like creatinine and urea, appear to be end products of metabolic processes and must be removed from the body,³ whereas others are essential to the construction of more complex compounds or to the development of energy for use by cells and must, therefore, be conserved. The kidneys are important in the maintenance of the plasma composition of many of these substances either by providing a route of active excretion or by preventing their loss in the urine.

Relatively little is known of the factors that govern the plasma concentrations of most of these compounds. The methods of chemical analysis are unsatisfactory and often difficult. In fact, a relatively large residue of organic material in the blood and urine remains unanalyzed. Moreover, the intracellular reactions in which organic compounds participate cannot be examined directly. Despite this paucity of knowledge, or perhaps because of it, there has been considerable speculation regarding their activity during renal insufficiency.

In general, these compounds fall into three groups from the standpoint of renal physiology. Large complex molecules that cannot pass the glomerular filter, such as proteins and fats, do not appear in the filtrate except during renal disease. Under these circumstances protein and lipoidal substances may be lost in the urine. In addition, it appears that abnormal renal cellular activity may provoke a general disturbance in fat¹²⁰ and protein metabolism¹²¹. A second group of substances, including glucose and the amino acids, appear in the glomerular filtrate and are so actively reabsorbed that little is lost in the urine. Curiously enough, an excessive loss does not usually occur even in advanced renal insufficiency. The third category, however, composed of diffusible waste products, including urea, creatinine and uric acid, is normally excreted in

large amounts in the urine and accumulates in the blood when the filtration rate is reduced.

The retention of organic catabolites in the blood during renal insufficiency was discovered shortly after Bright's demonstration of the relation between renal disease and uremia. The hypothesis that the symptomatology of uremia is based on an intoxication by these substances was immediately developed and has continued to occupy a prominent position in discussions of renal insufficiency. But little direct and trustworthy evidence has been brought forward in support of this thesis. Each of a number of substances has been advanced as the sole cause of symptoms. More recently, emphasis has been placed on the possibility that the retention of several toxic agents is involved.^{122, 123} It is tacitly or explicitly implied in most studies, however, that the uremic syndrome arises from a toxemia. In the light of the increasing knowledge of the metabolic imbalance during renal insufficiency, this viewpoint seems oversimplified. Certainly, the serious disturbances of body water and electrolytes must play a role in causing symptoms. Likewise, it seems probable that a general disorder of all metabolic activity, arising from the abnormalities of plasma catabolite concentrations among others, is involved. In this view, the increased concentrations of such substances as urea, creatinine, phenol and guanidine are important not because of the pharmacologic action of each but because of the interference with many intracellular reactions in which they participate. For this effect, none of them need be present in the blood in toxic amounts.

Nonprotein Nitrogen

It is well known that the nonprotein nitrogen content of the plasma increases, as a rule, with renal insufficiency. This change has come to be regarded as the hallmark of renal failure, although occasionally azotemia fails to develop even in far-advanced renal disease.¹²⁴

The nonprotein nitrogen of the blood is derived from many sources, among which urea, creatinine, uric acid and the amino acids are most significant. The plasma concentrations of these compounds, with the exception of the amino acids and possibly other substances that contribute little to the total nonprotein nitrogen, depend on a balance between tissue breakdown, intracellular metabolic processes and diet on the one hand and renal excretion on the other. Thus, azotemia develops when this balance is deranged by a failure of renal excretion or by an increase in the production of nitrogenous substances, or both.

Recent studies indicate that a negative nitrogen balance develops in the presence of unusual stress.^{125, 126} Excessive nitrogen loss, which occurs during fever, after trauma or operative procedures

and during shock, cannot be prevented by dietary measures¹²⁷ and is apparently not attributable to tissue destruction or disuse atrophy.¹²⁸ It has been suggested¹²⁹ that this phenomenon is related to Selye's¹³⁰ "alarm reaction" and may possibly be due to excess secretion of the so-called "S hormone" by the adrenal cortex. It is entirely possible that similar factors are operative in some cases of renal insufficiency and account, in part, for azotemia. Certainly, the characteristic wasting is attended by mobilization of nitrogen and negative nitrogen balances have been observed in chronic renal disease.¹³¹ From a therapeutic standpoint, it is interesting that desoxycorticosterone appears to retard the elevation of nonprotein nitrogen in nephrectomized rats.⁷¹

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centration reached a higher level than normal and returned slowly to the control value. Since no abnormality of the respiratory quotient was demonstrable, it was concluded that some factor other than a failure to burn glucose, such as retarded glycogen storage, was responsible. In the absence of renal failure the glucose tolerance was normal. This defect of carbohydrate metabolism is in line with the view that uremia arises from a general metabolic disturbance.

Amino Acids

The amino acids are also reabsorbed efficiently, and if retention occurs it apparently stems from an abnormality of liver function. Lyttle and his co-workers¹⁴³ have given intravenous injections of casein hydrolysate to children with renal disorders and have studied the rate of return of amino acids in the blood to a normal level. They found that normal removal from the blood occurred in spite of the presence of renal insufficiency. In children with hepatic disease and normal renal function, however, the removal of amino acid was greatly retarded.

In this study, it was found that the nephrotic syndrome was characterized by normal uptake of amino acids, in harmony with the work of others.¹⁴⁴ But an augmentation of amino acid removal from the blood has been observed shortly before the onset of the so-called "nephrotic crisis," with the subsequent development of hypoaminoacidemia.¹⁴⁵ The causes for the negative nitrogen balance and loss of amino acids in this situation are obscure. It appears that the parenteral administration of casein hydrolysate corrects the disturbance of nitrogen balance to some extent and apparently produces a significant reduction of fatalities due to bacteremia during the crisis.¹⁴⁶ Farr¹⁴⁴ attributes the loss of nitrogen to toxic nitrogen metabolism. It is not clear whether the loss of amino acids in the urine is a factor.

It should be understood that the methods now available for studying the amino acids of the blood are unsatisfactory and that what has been said about them has reference, for the most part, to the alpha amino acids detected by the ninhydrin method. Other methods are available for the determination of many individual acids. The use of these procedures in studies of the behavior of different acids during renal insufficiency should elicit much interesting information.

Phenols

The discovery that phenolic compounds accumulate in the blood during uremia has aroused considerable interest.¹⁴⁷⁻¹⁵⁰ These substances are believed to be derived largely from the degradation of aromatic amino acids in the intestine. Free phenols are extremely toxic, causing renal damage and central-nervous-system depression. Harrison¹²² sug-

gests that they are responsible for certain of neuromuscular phenomena observed in uremic animals. The methods used in determining the concentrations of phenols in the blood, however, are nonspecific and unreliable. The chief argument in favor of the importance of these substances in the production of uremia lies in the fact that a good correlation has been found between symptomatology and phenol accumulation. This need not imply a causal relation, however.

There is little evidence to support the view that other toxic products of intestinal putrefaction, such as indican, are of any significance in uremia.^{151, 152}

Plasma Proteins

Protein is lost in the urine throughout most of the course of renal insufficiency, probably owing to increased passage of large molecules through the defective glomerular filter, although there is evidence that diminished tubular reabsorption of protein is also at fault.¹⁵³ The character of the urinary protein complies with the view that an increase in the size of glomerular pores permits smaller species of protein molecules, particularly albumin, to escape from the plasma. When this loss is excessive, hypoproteinemia develops. It appears that urinary loss is not sufficient to account for the diminution of protein in most cases, however, and a disturbance of protein manufacture must be posited.¹⁵¹ Since protein escape is reduced by the contraction of the glomerular filter bed with progressive renal damage, hypoproteinemia is gradually corrected, and during the terminal stages of uremia, it is not a prominent feature.

The study of the plasma proteins is still in its early stages. New methods have been developed and have not yet been extensively applied to the investigation of renal disease.

Lipids

It has been shown that renal damage not only permits the escape of lipoidal compounds in the urine but also leads to lipemia and hypercholesterolemia. For reasons as yet unknown, this disturbance of fat metabolism is most profound in the presence of hypoproteinemia and may be related to it in some way. As renal failure progresses, these abnormalities regress.^{120, 154, 155}

* * *

Throughout this discussion, an effort has been made to emphasize the complex nature of biochemical disturbances during renal insufficiency. This complexity arises from the simultaneous derangement of metabolic activities of all types throughout the body and is secondary to the disorder of plasma composition resulting from the failure of the kidney to perform its regulatory functions. It is probable that the symptomatology of uremia is the result of the action of multiple

factors, among which the change in the character of the metabolic pool bulks large

The attempt to find toxic agents retained by the diseased kidney to account for various symptoms has not been fruitful. No evidence that the kidney manufactures toxic substances has been elicited,¹³⁶ and the evidence suggesting that intoxication by products of intestinal putrefaction occurs is not convincing. It may be that substances as yet undetermined play an important role, but there seems to be ample cause for symptomatology in the disturbances that have been subjected to quantitative study.

Obviously a considerable amount of work remains to be done. At present, the factual knowledge of normal processes is faulty and incomplete, and it is not surprising that a satisfactory understanding of the abnormalities has not yet been attained. As methodology improves and factual data accumulate, however, rapid strides on the conceptual level may be confidently expected.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32481

PRESENTATION OF CASE

First admission A thirty-eight-year-old Italian clerk entered the hospital because of a swelling below the right eye, which he suspected of being a "cancer."

For three years before entry the patient had noticed many small, spidery, red spots on the cheeks, abdomen and flanks. These never increased in size or caused him any concern until two months before entry, when one of these spots beneath the right eye began to enlarge. Except for this condition, the patient considered his health excellent. He had had a slight, nonproductive cough following an attack of pleurisy eighteen years previously. Since the age of nine years he had also had an occasional slight purulent discharge from the right ear. He had observed no swelling of the abdomen, jaundice, hemorrhoids, varicose veins or ankle edema. The alcoholic intake was impressive, amounting to at least a bottle of wine a day since childhood and an additional daily consumption of about a quart of whiskey and several bottles of beer for the preceding eight years. Nevertheless, he insisted that his diet was "good" and his appetite keen. The weight had remained constant for

the past seventeen years. The urine had been orange on occasion, but the stools had always been brown.

The patient was a well developed and well nourished man with fine spider angiomas over the chest, upper abdomen and flanks. Below the right eye there was an angioma 2 cm. in diameter with a slightly raised red antrum 3 mm. in diameter. The heart and lungs were clear. The abdomen was protuberant and soft, with a questionable fluid wave but no shifting dullness. The liver edge was readily palpable, extending 12.5 cm. below the costal margin in the anterior axillary line, but was firm and nontender.

The temperature, pulse and respirations were normal. The blood pressure was 140 systolic, 85 diastolic.

The blood van den Bergh reaction was 27 mg. per 100 cc. total. The cephalin-flocculation test was ++++ at the end of twenty-four hours. A bromsulfalein test showed 35 per cent retention of the dye. The total serum protein was 7.6 gm. per 100 cc., with an albumin-globulin ratio of 1.5. The urine gave a ++++ test for bile and green, blue and orange reactions for sugar on three occasions. The stools were guaiac negative.

A gastrointestinal series and chest plates were essentially negative.

Peritoneoscopy revealed a large "hobnail" liver, and a biopsy specimen was reported as showing advanced toxic cirrhosis.

The patient was discharged with instructions to abstain from alcohol and to follow a high-vitamin, high-carbohydrate, high-protein, high-calorie and low-fat diet.

Final admission (four and a half years later) The patient was followed in the Out Patient Department and apparently did well although he noticed slight swelling of the ankles at night, he had a dirty-gray color. He claimed to have restricted his drinking to about four highballs a day. A month before entry he began work as a night watchman and

felt unusually tired and sleepy. On the day of entry, he developed chills and fever while at his job and was brought to the emergency ward via ambulance. On arrival he also noted "dizziness" and swaying from side to side while walking. The right ear had recently been draining purulent material, but this was no different from many previous episodes.

The patient appeared acutely and chronically ill. He was drowsy and dozed off several times during the examination. The skin was hot and dry and showed a grayish icteric pigmentation, most marked in the exposed areas. There were numerous spider angiomas. A skin test for iron pigment was negative. The pharynx and soft palate were beefy red, with a mucous coating over the posterior portion. The right ear canal contained blood-tinged, seropurulent discharge. There were a few rales at the left base. A Grade II apical systolic murmur was transmitted over the entire precordium. The aortic second sound was louder than the pulmonic. There were shifting dullness over the abdomen and a questionable fluid wave. The liver edge was palpable 4 fingerbreadths below the costal margin. Moderate muscle weakness was apparent in all extremities, and vibratory sense in the legs was absent.

The temperature was $100\pm^{\circ}\text{F}$, the pulse 100, and the respirations 24. The blood pressure was 110 systolic, 60 diastolic.

Examination of the blood showed a red-cell count of 4,840,000, with 15 gm of hemoglobin, and a white-cell count of 20,200, with 92 per cent neutrophils. The fasting blood sugar was 190, the non-protein nitrogen 30 and the phosphorus 2.5 mg per 100 cc, the alkaline phosphatase was 6.1 Bodansky units per 100 cc, the sodium 128.4 milliequiv per liter and the serum protein 5.8 gm per 100 cc, with an albumin-globulin ratio of 0.8. The van den Bergh reaction was 5.6 mg per 100 cc direct and 10.0 mg total. The cephalin-flocculation test was ++++ in twenty-four hours. The prothrombin time was 30 minutes, with a control of 18 minutes. *Staphylococcus aureus* was grown on two consecutive blood cultures. The urine was dark amber, with a specific gravity of 1.014. There was a green test for sugar and a ++ test for bile but no albumin. The sediment contained many white cells, red cells and granular casts per high-power field.

An x-ray film of the chest showed enlargement of the heart, particularly in the region of the left ventricle and left auricle. The diaphragm moved only slightly. The lung fields were clear. There was a suggestion of small varices in the lower third of the esophagus.

An electrocardiogram showed a rate of 95, with sinus rhythm. The PR interval was 0.18 second and the QRS complex 0.08. The voltage was normal, and there was no deviation of the axis. The T waves in Leads 1 and 2 were unusually broad and rather low.

The temperature gradually returned to normal on penicillin therapy, but the pulse rate was continuously elevated, the patient frequently lapsed into a semicomatose or delirious state. The dosage of penicillin was 24,000 units every three hours for six days and was increased to 32,000 units every two hours for the remainder of the illness. A lumbar puncture showed an essentially normal fluid with normal dynamics. During the ten days in the hospital the patient gained 22 pounds, which was apparent as pitting edema over the dependent portions and increasing ascites. On the seventh hospital day a Grade II diastolic murmur to the left of the sternum was discovered. The patient was digitalized and given Mercupurin. Nevertheless he continued to gain fluid. A Prussian-blue skin test for hemochromatosis was negative in two injection sites. On the sixteenth hospital day the patient was found unresponsive, with Cheyne-Stokes respirations, and he died shortly thereafter.

DIFFERENTIAL DIAGNOSIS

DR. JAMES TOWNSEND: There is no record of a blood sugar determination or a blood Hinton test during the first admission four and a half years previously or of any test for sugar in the urine in any of the visits to the Out Patient Department between the admissions. Certain things in the clinical history are worthy of emphasis. The alcohol intake described is enormous, amounting to 6000 calories a day. Under these conditions it is improbable that the patient had a normal food intake, and he might therefore be considered a fit subject for avitaminosis. Secondly, spider angiomas were noticed on both admissions. These, if typical, are important findings, believed by many to be pathognomonic of Laennec's cirrhosis, but I am sure that they occur in other types of liver diseases, the most characteristic ones that I have seen occurred in a case of prolonged infectious hepatitis that began during an epidemic among the American forces in Italy. Thirdly, convincing evidence of toxic cirrhosis four and a half years previously was provided by the various chemical tests as well as by direct vision of the liver and biopsy. The chemical findings at the time of the final admission are consistent with a gradual progression or recent exacerbation of the cirrhosis. Fourthly, there was definite evidence of enlargement of the heart since the first hospitalization, as well as new murmurs, both systolic and diastolic, not previously described. Finally, the finding of a low serum sodium is worthy of note. There are two conditions that are usually associated with a low sodium—Addison's disease and severe dehydration. In this case there is no evidence of dehydration.

It seems to me that the following were the most significant findings in this long and rather complicated picture. A definite diagnosis of toxic cirrhosis was made four and a half years before the final entry, with evidence of progression of the disease during

the illness as shown by the ascites, the hypoproteinemia and the possible esophageal varices and of glycosuria at that time and during the final illness. Could the last finding be attributed to cirrhosis? There is a carbohydrate disturbance in cirrhosis, but — except after the injection of glucose — sufficient sugar in the urine to give an orange reaction is unusual. It would be extraordinary to have a fasting blood sugar as high as 190 mg per 100 cc. Therefore, I believe that this man had diabetes, probably of several years' duration, and that autopsy may have revealed some of the findings that are found in patients with chronic diabetes, usually in the vascular system, with the glomeruli showing changes characteristic of Kimmelstiel-Wilson disease and other vascular disturbances. The patient had a chronic middle-ear infection for many years, and the symptoms of acute illness began a month before the final admission, when he had fever and a discharge from his ear that increased on the day of entry. He was given a course of penicillin. New heart murmurs, both systolic and diastolic, were noted, with cardiac enlargement that had not been present four years earlier, and *Staph aureus* was grown on two blood cultures. He also had abnormal urinary findings, but without albumin, and a normal nonprotein nitrogen.

There seems to be no room for argument against cirrhosis of the liver. The clinical picture was quite characteristic, and I think we may assume that the disease either progressed in spite of treatment or became exacerbated during the final illness. I believe that the patient still had severe cirrhosis of the liver of the Laennec type. Could it have been some other type? This man had the triad of peculiar color of the skin, diabetes and liver disturbances. Hemochromatosis comes to mind. Tests were done for that, but they were negative. There was even a negative skin biopsy, and I doubt whether hemochromatosis was apparent clinically. In the few cases that I have seen the only characteristic finding has been severe diabetes, which is difficult to control in spite of large doses of insulin. If this man had diabetes, it was mild and chronic. I believe that he had diabetes mellitus in addition to the cirrhosis of the liver.

He also had a chronic suppurating process in the right ear, which I believe had much to do with the onset of the final illness. I should like to believe that it was the portal of entry of the *Staph aureus* that was found in the blood stream. There is considerable evidence to support the diagnosis of bacterial endocarditis because of the finding of new heart murmurs, the presence of cardiac enlargement and the progressively fatal course in spite of a fair amount of penicillin. If he had bacterial endocarditis, other areas of staphylococcal infection may have been observed in the kidneys and possibly in the liver or the brain, or almost anywhere in the body.

What shall we expect to find in relation to this ear? We are not given much detailed information. All we know is that the patient had had a discharging ear for a long time. He also had diabetes and cirrhosis and low resistance, however, and I suspect that this septic process was extending inward and that it had something to do with the later illness. I assume that he had involvement of the internal ear or that he had an abscess, possibly extradural or in the brain. He did not have meningitis, because the spinal fluid was normal. On the evidence at hand we cannot exclude the possibility of brain or extradural abscess or lateral sinus thrombosis. This is merely speculation, but these are the conditions that are apt to occur from chronic suppurating ears.

Finally, the illness was associated with a *Staph aureus* infection of the blood stream, which I believe was localized in the heart valves — certainly the aortic and possibly the mitral.

Did the patient have any other disease, such as a superimposed kidney lesion of some sort? He retained a tremendous amount of fluid during the last few days, and in that retention of fluid there may have been several elements. He probably had some degree of portal obstruction that encouraged ascites. He may have had some cardiac failure, although the clinical picture was not characteristic, as well as a kidney condition that encouraged the retention of fluids. The urine showed white cells, red cells and casts, but no albumin. There are at least three types of disease that might be found in such a case. A diffuse glomerulonephritis, which is the first type, almost always shows large amounts of albumin. The other types are the changes of intercapillary glomerulosclerosis and abscesses from staphylococcal septicemia.

The diagnoses that I suspect may be found are cirrhosis of the liver (Laennec type), diabetes mellitus, chronic suppurative otitis media, staphylococcal septicemia, bacterial endocarditis, embolic abscesses of the kidney or other organs, possible lateral sinus thrombosis, possible brain abscess and possible glomerulonephritis.

CLINICAL DIAGNOSES

Portal cirrhosis
Hemochromatosis?
Staphylococcus aureus sepsis

DR. TOWNSEND'S DIAGNOSES

Cirrhosis of liver, Laennec type
Diabetes mellitus
Otitis media, chronic suppurative
Staphylococcal septicemia
Bacterial endocarditis
Embolic abscesses, of kidney or other organs
Lateral sinus thrombosis?
Brain abscess?
Glomerulonephritis?

ANATOMICAL DIAGNOSES

Acute bacterial endocarditis (due to Staphylococcus aureus), with rupture of aortic valve

Hemochromatosis

Bicuspid aortic valve

Septic infarct of kidneys and spleen

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN Autopsy showed a number of findings that Dr. Townsend predicted. The heart was enlarged, weighing over 400 gm. The enlargement was probably due to a mild degree of aortic stenosis. There was a bicuspid aortic valve, as well as calcific deposits of a mild degree along both cusps. Superimposed on the deposits of calcium were grayish, pink vegetations — an acute bacterial endocarditis that had perforated both cusps. There was also a small focus of bacterial endocarditis on the mitral valve.

The liver weighed 1200 gm. and showed a severe hobnail type of cirrhosis. The color of the liver was pale brown, verging on orange, which is a color often seen when there are deposits of hemosiderin in the liver, and this was confirmed by a positive Prussian-blue reaction for iron. Although the presence of hemosiderin does not always mean hemochromatosis, a history of diabetes in addition to the finding of a uniformly deep-brown pancreas filled with hemosiderin makes the diagnosis of hemochromatosis quite definite. The pancreas was not extremely fibrous but perhaps more so than normal, and the color was certainly that seen in bronze diabetes, also, many of the regional lymph nodes were brown. We can assume that the patient did have hemochromatosis. We reviewed the original biopsy taken four and a half years previously, and that did not show hemochromatosis. It was a fairly adequate biopsy and revealed definite portal cirrhosis. This is an important case in relation to the pathogenesis of hemochromatosis. Most people believe that the initiating factor in the cirrhosis of hemochromatosis is the pigment — that is, the pigment stimulates fibrosis first in the liver and then in the pancreas. Another theory of the pathogenesis of hemochromatosis is that cirrhosis of unknown cause appears first and the iron from the normal blood destruction is abnormally metabolized. Deposits of iron in the liver were therefore superimposed on a previous cirrhosis. This case certainly fits in with this theory.

DR. TOWNSEND Did the other endocrine organs, such as the adrenal glands, show hemochromatosis?

DR. CASTLEMAN No. The involvement was not so diffuse as that in the usual cases of hemochromatosis. Quite possibly it was not present long enough.

DR. TOWNSEND This is probably why the patient's skin had a queer color. He was not given the clinical skin test?

DR. CASTLEMAN Not by the injection method. It is possible that the biopsy might have shown a

Prussian-blue reaction. The kidneys contained hemorrhagic septic infarcts.

DR. TOWNSEND The kind that occurs with *Staph. aureus*?

DR. CASTLEMAN Yes. Two small infarcts in the brain accounted for most of the cerebral symptoms.

DR. TOWNSEND Was there any local disease around the ear?

DR. CASTLEMAN No, there was no severe involvement of the middle ear, and no sinus thrombosis.

CASE 32482

PRESENTATION OF CASE

A thirty-four-year-old unmarried woman, a typist, was admitted to the Neurological Service because of severe pain in the right leg.

Six months before admission the patient had been operated on because of prolonged excessive vaginal bleeding of two months' duration, there had been three episodes of severe low abdominal pain during this period. At operation both tubes and bloody cysts of both ovaries were removed. Fifteen days after operation a sudden, severe right-sided "sciatica" had occurred, after which the pain had been constant. It ran from the hip into the right leg, down to the heel and sometimes up the spine. Between the severe, sharp bouts it was present as an ache. At the time of the menstrual periods, the pain was worse. It was not aggravated by coughing, sneezing or straining. X-ray studies of the chest and hip were negative. After operation there was no intermenstrual bleeding. The periods were regular and extremely painful. The pain was largely in the left lower quadrant. The distress made the patient nervous and apprehensive, and she was often nauseated. She had lost 5 pounds in weight.

Physical examination showed an undernourished and anxious woman. There were tenderness and voluntary spasm in the left lower abdominal quadrant. The right leg was slightly weaker than the left, and straight-leg raising was limited to 45° on that side. The cervix was large and soft. The uterus was retroverted, partially fixed and enlarged. Any movement of the cervix or uterus caused severe pain. A cystic mass was palpable in the posterior cul-de-sac. Rectal examination confirmed the fixation of the uterus and the presence of a hard mass off the left side of the cervix and uterus.

Examination of the blood revealed a red-cell count of 4,010,000, with a hemoglobin of 12.6 gm., and a white-cell count of 8600. The urine gave a + test for albumin, and the sediment contained 3 to 30 white cells and 1 red cell per high-power field. The sedimentation rate was 2 mm. in fifteen minutes, 7 mm. in thirty minutes, 14 mm. in forty-five minutes and 19 mm. in sixty minutes. X-ray studies of the chest, spine and kidneys were negative. In the intravenous pyelogram the lower ureters diverged

somewhat laterally, and there was pressure on the superior margin of the bladder, probably from an intrapelvic mass, which could not be outlined.

An operation was performed on the fifth day.

DIFFERENTIAL DIAGNOSIS

DR. MARSHALL K. BARTLETT There are a number of points of interest in this history. In the first place, of course, one would like to know the nature of the ovarian cysts removed six months before entry. What kind of lesion could have caused the surgeon to remove both tubes and bilateral ovarian cysts in a thirty-four-year-old unmarried patient? Simple cysts of the ovaries might contain bloody fluid and give the type of vaginal bleeding that this patient had. The duration of trouble before the first operation was brief, but there was no previous mention of dysmenorrhea. We know that there were three episodes of severe pain low in the abdomen during that period. Were the cysts endometriosis? That certainly comes to mind promptly in an unmarried patient of thirty-four who has menstrual difficulties. Were they malignant cysts? I think that we can go far enough to say that if they were malignant the fact was not recognized at the time of operation, otherwise, that type of procedure would not have been done. Certainly, removal of the cysts and the tubes would not be considered adequate surgery if the lesion had been recognized as malignant. I do not see how we can decide the exact nature of the cysts.

The next thing of interest is the onset of severe right-sided "sciatica" fifteen days after operation. Was that due to an underlying lesion in the pelvis? It is hard for me to accept that as the principal cause. It seems to me that if this had been a development of a process in the pelvis the onset would have been more gradual and more insidious. The distribution suggests involvement of the sacral nerve roots. The pain was continuous, with acute exacerbations throughout the interval, until admission to the hospital. It is stated that the pain in the back and leg was worse at the time of the periods. I cannot attach too much significance to that, because almost every patient with backache asserts that it is worse at the time of a period. I am therefore inclined to discount the statement.

X-ray studies of the chest and hip were negative. The periods were regular, with no further intermenstrual bleeding. In other words, normal ovarian tissue must have been left behind at the operation—at least enough so that the patient was able to have regular periods. The periods were painful. Again, it would be interesting to know how much dysmenorrhea she had had before the first operation. In any case, in the interval between the two operations, the periods were painful, and the pain was chiefly in the left lower quadrant. On admission it was noted that the right leg was slightly

weaker than the left. One would like to know if that muscle weakness was generalized, involving all the muscle groups, or perhaps limited to certain muscle groups. Certainly at that time there was a pelvic lesion of some kind, with a palpable mass. Was the original lesion a pelvic inflammation and was this episode a recurrence? It seems unlikely to me, because the tubes had been taken out at a previous operation for pelvic inflammation. That should have cured her. Were the cysts that were removed simple ovarian cysts? Again, it seems to me that the patient should have been cured by the first operation and should not have gone on to develop a further pelvic lesion, or at least not so promptly. Were they malignant ovarian cysts, with recurrence in the pelvis? I do not see any way that I can rule that out. She was rather young, which is somewhat against it. I think that if the disease had been recognized as malignant she should have had more extensive surgery at the original procedure.

Could recurrence of malignant disease in the pelvis cause the back pain? I think that it could on the basis of metastases. We have no x-ray evidence to support that. Could this process in the pelvis have been endometriosis? Certainly, the patient was in the right age group. She was nulliparous and it seems like a good bet. If the first operation was done for that reason, a conservative procedure would be justified in a patient of her age, although the removal of the tubes, of course, would not be desirable. It would account for the recurrent process in the pelvis with dysmenorrhea in the interval between operations. Can we explain the back pain on that basis? I cannot remember seeing a patient with back pain of this type due to endometriosis. I am rather inclined to believe that the back pain had no relation to the process in the pelvis. As my first diagnosis, I shall put endometriosis as the cause for the underlying disease, with a malignant lesion in the pelvis as a second choice.

DR. TRACY B. MALLORY Dr. Ingersoll, you were present at the operation, will you describe the findings?

DR. FRANCIS M. INGERSOLL I was not present, but I heard about it. The patient had been operated on previously. At operation the surgeon found what can best be described as a "frozen pelvis"—so frozen that operation was a difficult technical procedure. Behind the sigmoid on the left side, there was a cystic mass and the sigmoid mesentery formed one of its walls. In freeing up the sigmoid three holes were made in it, which I mention simply to demonstrate how difficult it was to free the sigmoid and straighten out the situation in the pelvis. There was a cyst not related to the ovary on the right side. Since it was apparent that an extensive endometriosis was involved, the surgeon removed the uterus and the remnants of the ovaries and did a colostomy, exteriorizing the sigmoid.

CLINICAL DIAGNOSIS

Endometriosis
Pelvic inflammation?
Carcinoma of ovary?

DR. BARTLETT'S DIAGNOSIS

Endometriosis

ANATOMICAL DIAGNOSIS

Endometriosis.

PATHOLOGICAL DISCUSSION

DR. MALLORY The specimen that we received in the laboratory showed extensive endometriosis of the remaining fragments of the two ovaries and of the posterior surface of the uterus. There is very little doubt that the wall of the sigmoid would have shown the same process if we had received a specimen from it. These cases of endometriosis involving the sigmoid often make a difficult surgical problem. In a certain number of cases the surgeon has mis-

taken the lesion for a primary carcinoma of the bowel and has done extensive resection. In cases in which the lesion has been correctly diagnosed at operation, it has frequently been possible with a colostomy to tide over the temporary intestinal obstruction, perform a surgical castration and later take down the colostomy and find that the intestinal obstruction has been relieved. The endometriosis atrophies spontaneously once the ovarian function has been destroyed.

DR. BARTLETT Do you know what caused the pain in the back?

DR. HOWARD ULFELDER The patient is much better, but of course she has been on bed rest since the operation.

A PHYSICIAN Is it possible to explain the pain on the basis of pressure on the ureters?

DR. MALLORY It was impossible at operation to recognize either ureter. Both ureters were buried in scar tissue and may well have been involved, although that would have been an unusual reference of pain, would it not?

DR. ULFELDER I should think so.

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INCREASE IN MORBIDITY DUE TO DIPHTHERIA

A NOTE from the Massachusetts Department of Public Health, appearing elsewhere in this issue of the *Journal*, indicates that there has been a marked increase in diphtheria in Greater Boston during 1946, a considerable portion of which has occurred since September 1. In recent years diphtheria has become a rare disease in Massachusetts, and during the past decade many physicians have not even had the opportunity of studying clinical cases during the time of their medical-school training. Control of this infection has been attributed largely to immunization programs that have been universally adopted throughout the Commonwealth.

Preliminary laboratory reports have demonstrated that the diphtheria bacilli recovered from many of the cases in the Greater Boston area during September were the gravis type. Studies published in 1944 suggested that such strains are associated with a malignant variety of clinical diphtheria with a considerable proportion of infections of the so-called "bull-neck" variety,¹ but this observation has not been confirmed in Massachusetts.² Thus, in a recent outbreak from which the gravis type of diphtheria bacilli was recovered, the majority of cases had an extremely mild clinical course. This confirms the conclusion of Frobisher³ that clinically severe diphtheria is only irregularly associated with the gravis type of organism, which is not of itself sufficient to cause malignant diphtheria.

In Canada recent statistical studies have indicated a change in the age distribution of diphtheria, and in one reported epidemic it was found that 45 per cent of the cases occurred in persons over fifteen years of age.^{4, 5} In Massachusetts, during 1945, 44 per cent of the cases were in the same age group, and in the three preceding years, at least 45 per cent of all reported cases occurred in persons who were ten or more years old.²

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Formerly

The Boston Medical and Surgical Journal

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INCREASE IN MORBIDITY DUE TO DIPHTHERIA

A NOTE from the Massachusetts Department of Public Health, appearing elsewhere in this issue of the *Journal*, indicates that there has been a marked increase in diphtheria in Greater Boston during 1946, a considerable portion of which has occurred since September 1. In recent years diphtheria has become a rare disease in Massachusetts, and during the past decade many physicians have not even had the opportunity of studying clinical cases during the time of their medical-school training. Control of this infection has been attributed largely to immunization programs that have been universally adopted throughout the Commonwealth.

Preliminary laboratory reports have demonstrated that the diphtheria bacilli recovered from many of the cases in the Greater Boston area during September were the gravis type. Studies published in 1943 suggested that such strains are associated with a malignant variety of clinical diphtheria with a considerable proportion of infections of the so-called 'bull-neck' variety,¹ but this observation has not been confirmed in Massachusetts.² Thus, in a recent outbreak from which the gravis type of diphtheria bacilli was recovered, the majority of cases had an extremely mild clinical course. This confirms the conclusion of Frobisher³ that clinically severe diphtheria is only irregularly associated with the gravis type of organism, which is not of itself sufficient to cause malignant diphtheria.

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CARL BEARSE, *Chairman*

A HUNDRED YEARS AGO

It has long been an important problem in medical science to devise some method of mitigating the pain of surgical operations. An efficient agent for this purpose — inhalation of ethereal vapor — has at length been discovered. The process is obviously adapted to operations which are brief in their duration, whatever be their severity, and it may hereafter prove safe to administer it for a length of time and to produce a narcotism of an hour's duration. — We learn that a disgraceful fight took place on Sunday noon last between the Freshmen and medical students of Dartmouth College. It took place as they were leaving the church. — We apprehend that rectum bougies are not resorted to as frequently as they might be with striking manifestations of advantage to the patient. There is a fashion to be followed in the treatment of chronic diseases as well as in the cut of a coat. The surgeons of thirty years ago derived much more assistance from these very instruments, though of inferior manufacture, than their successors of the present day. — It is spoken of as a matter already settled that Dr Wm Lawrence of Boston, who has lately returned from Europe, has purchased the old Medical College in Mason Street which is to be fitted up for an Infirmary for children and infants. — On Wednesday last, the new edifice of the Medical College near the Massachusetts General Hospital in Grove Street was formally opened by an address from the President of Harvard University, who was particularly happy in his remarks upon the social position of medical practitioners, their duties, and their philanthropic exertions. Every person present must have been gratified with his observations, clothed as they were, in beautiful language. — If students of medicine are not well taught in this age, there must be some defect in themselves. It is a subject of perfect surprise to us that a single stupid fellow can be found in a lecture-room or office, surrounded as he must be continually by an atmosphere of science. — A boy aged 7 years received a wound between the 7th and 8th ribs by a thrust from a narrow but long-bladed knife. Three weeks and four days from the accident, he was taken with a sudden and fatal syncope. A cicatrix of the size and form of the knife-blade was found on the pericardium. There was an opening in the anterior coronary artery. The patient would have recovered perfectly if sloughing of the coronary had not taken place. Such cases do recover in all probability. We hear of cases where buffaloes have been killed, and rifle or musket balls found lodged in the substance of the heart, having entered a long time previous to death. — A slave recently died at Frankfort, Ky., at the age of 112 years. When 84 years of age, he married his fourth wife, and raised a family of 7 children. — Another important discovery has been

made in the manner of preparing gold for dental purposes. Dr Charles T Jackson, a gentleman who takes the first rank in chemistry, has prepared pellets of pure gold, almost as flocculent as wool, which only require a slight degree of manipulation to fit them to the ragged interior of a tooth, without pain, and with so slight a pressure as to make no disturbance in the region. Those who have borne the heavy pressure of the dental operator's punches and the fatigue of being belabored scientifically to save a few diseased teeth will welcome the new process with marked pleasure and interest. — An Aesculapian Society, entirely made up of medical students attending lectures in New York has commenced weekly sessions for the season. — Extracted from the *Boston Medical and Surgical Journal*, November, 1846

R. F

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

DIPHTHERIA ON THE INCREASE

Recently the Boston Health Department, in a letter addressed to physicians in Boston, pointed out that there has been an increase of diphtheria cases in that community. A similar and more striking rise has been noted in the adjoining community of Somerville. Diphtheria case rates for the two cities since 1940 are shown in the following table

YEAR	BOSTON	SOMERVILLE
1940	2 075	9 786
1941	2 075	2 936
1942	2 075	7 829
1943	4 670	17 616
1944	6 486	45 998
1945	5 967	20 552
1946 (8 months)	9 470	26 424

The case rates are per 100,000 population, based on 1940 United States Census

Since January 1, 1946, a total of more than 161 cases have been reported in the Greater Boston area, and 79 of these have occurred in Boston and Somerville during September and the first eleven days in October. It is expected that cases will continue to appear at an increased rate in this area until the effect of intensified diphtheria immunizations will have become manifest. The letter suggests that physicians bear in mind the possibility that diphtheria may occur more frequently now than it has in the past. Delay in diagnosis and tardy administration of antitoxin have been factors in the fatal outcome of several cases.

The increased incidence has been called to the attention of all boards of health in the Greater Boston area, with the recommendation that diphtheria immunization programs be strengthened. Booster doses for children previously immunized are being suggested in Boston, Somerville and the adjoining communities.

It is impossible to predict the area in which the disease will appear next. For this reason each community in the Commonwealth is being warned to take stock of its diphtheria immunization program, with immediate steps to forestall a similar rise in prevalence. The regular immunization program is as follows:

- 1 Primary immunization of all children in the first year of life—three doses of diphtheria toxoid (0.5, 1.0 and 10 cc.) Any children not immunized then should be given toxoid at the earliest opportunity.
- 2 A booster dose (0.5 cc of toxoid) at entrance to school if primary immunization was done more than two years previously. The same booster dose for children in grades up to high school who did not receive a booster dose on entrance to school in previous years.
- 3 If high-school children or adults are to be immunized a Schick test should be performed. Susceptibles should be given toxoid in divided doses, beginning with 0.1 cc. Routine booster doses are not recommended for adolescents and adults. Combined diphtheria-pertussis and combined diphtheria-tetanus immunizing agents can be used for primary immunizations and for booster doses. These products are not yet available through the department.

In the present emergency it is recommended that a booster dose be given to all preschool children if more than two years has elapsed since primary immunization.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	December 2	Paul W. Hugenberger
Haverhill	December 4	William T. Green
Lowell	December 6	Albert H. Brewster
Greenfield	December 9	Charles L. Sturdevant
Gardner (Worcester subclinic)	December 10	John W. O'Meara
Springfield	December 10	Garry deN. Hough
Brockton	December 12	George W. Van Gorder
Fitchburg	December 18	Frank A. Slowick
Hyannis	December 19	Paul L. Norton
Worcester	December 20	John W. O'Meara
Fall River	December 30	David S. Grice

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments.

MISCELLANY

NOTE

The appointment of Dr. Hugo Muench, a former staff member of the International Health Division of the Rockefeller Foundation and professor of biostatistics at the Harvard School of Public Health, as head of the Department of Biostatistics, was recently announced by Dr. James S. Simmons, dean of the School. Dr. Muench is also assistant dean.

FURTHER EVIDENCE CONCERNING THE DANGERS OF DEMEROL

An editorial in the August 8 issue of the *Journal* called attention to the dangers of addiction following the use of Demerol, an article by Paul De Kruif in the June issue of *Reader's Digest* notwithstanding. Further evidence of the habit-forming possibilities of the drug is given in a letter "Experience with Demerol in Europe," by Dr. Max Samter, of Chicago, which was published in the September 28 issue of the *Journal of the American Medical Association*. It is repeated below to re-emphasize the dangers that may result from the use of this drug.

To the Editor—The following observations may be of interest to you with regard to the controversy between Dr. C. K. Himmelsbach, Chicago, Mr. H. J. Anallinger, Washington, D. C., and Paul de Kruif, Ph. D., Holland, *MICH. (THE JOURNAL, September 7)*.

In the spring of 1945 I acted as liaison officer between First Army Headquarters and a central "German Sanitary Staff" established temporarily to maintain the function of the large number of captured German medical installations. Repeated inspections of hospitals and numerous trips throughout the occupied area gave me an opportunity to become familiar with administrative and technical experiences and difficulties encountered by the German army.

A tragic accident led me to investigate the use of Demerol by the medical department of the German units then under our control. Allied troops which had opened a medical depot found a large stock of an alcoholic preparation of Dolantin (the German trade name for Demerol) mistook it for a beverage and drank numerous bottles, a large number of casualties resulted.

Consultation with German medical officers and pharmacists revealed that the staff had at this time 40 cases of known Demerol addiction in its files; that furthermore, a large number of hospitals had abandoned its use for this reason. It is interesting to note that in Germany too it had been assumed for some time that Demerol was less addicting than morphine—a theory which had been revised by the spring of 1945.

Subsequently I was called repeatedly by military government officials to examine cases of Demerol addiction in civilians. I remember 1 instance which illustrates convincingly the danger of the drug. A physician addicted to morphine submitted twice to treatment. After the second treatment he was advised to try Demerol and developed within three months an addiction to the substitute. During this period he performed an abortion and was committed to a sanatorium for clinical study. After several weeks an attempt to withdraw the drug was made; he developed no symptoms of withdrawal. It was suspected therefore, that he had managed to obtain considerable quantities of the drug. Careful isolation revealed not only that his wife in weekly visits had issued Demerol to him but that she herself—after having taken the drug once or twice as a sedative following her husband's confinement—had become a Demerol addict.

Although the case histories on pages 43 and 44 of the September 7 issue of *THE JOURNAL* contain convincing evidence against Paul de Kruif's statement it might be helpful to add these experiences to the warning.

MAX SAMTER, M.D. Chicago

CORRESPONDENCE

THE HOSPITAL INTERN

To the Editor—Everyone concerned in the patient-doctor-hospital relation stands to gain by a more cordial affinity between staff physician and intern. The visiting physician seems to have become inured to the lowly intern as an ornate figure in white that the hospital has hired and stationed as silent sentry. Instead of taking full advantage of an enthusiastic scholar fresh from the portals of medical learning, the intern is by-passed in the doctor's care of private patients and completely deleted from their management. Both are the losers in such an aloof and lowly arrangement. Hence the intern's year often passes without the establishment of close contact with the physician, for which he yearns and is justly entitled. He is allowed to pursue his tenure in white as a superlative and superfluous hospital attaché, who must of necessity be allowed to complete his requirements for licensure.

One junior colleague's choleric comments aptly reflect a general attitude. In being brushed aside by the doctor and patient as well, he sputtered "Nuts to them! If I'm not good enough for him or his patient, I'll sit my year out until I'm good enough for patients of my own." And he quickly added, "He can do his own scout work, he'll not get any more out of me than I have to give."

The intern is in a logical position to lighten the load of routine for the staff physician's hospital practice. For example, a convenient plan, followed by some, is to make the acquaintance of the intern at the beginning of his month on the service. During a friendly chat the intern is made cognizant of one's type of practice and exactly what is expected. He is made to believe that the doctor's success is, in part, directly dependent on him. As a junior partner, his ability is equally important to the older man's skill in patient management.

One method of giving the intern concrete information is handing him at this time a small card on which are recorded routines, orders and special idiosyncrasies that the staff man may have. Such a fraternal display of friendliness will win over any intern to his staff man, making him a willing understudy and servant. After such an initial relation the intern takes a personal interest and responsibility in each patient.

He is given the information necessary for leaving initial orders should the chief be unavailable, he calls for special orders and advises of the patient's admission status.

Added to this time-saving factor of relieving the staff man of admission orders are meticulous work-ups and accurate diagnoses. By thus taking the intern under his wing, the physician ensures these, his understudy does not wish to have faith broken in him when once it has been entrusted. Instead of a *laissez faire* attitude in his intern, the chief will note a thorough, conscientious one with precision in examinations. The intern may find items that the staff physician, in the hurry to get the patient hospitalized, has casually overlooked — physical findings of inestimable value in the case or precautionary measures that may obviate complications. In reality, an attending man's reputation lies in the band of the intern. It is enhanced by the loyal junior, whose enthusiastic remarks to the patient regarding the excellent care his doctor renders ensure respect and reliance.

Hospital rounds can be expedited by the intern. Nothing is more flattering to the intern than to have his senior walk up on the floor and ask, "How are our patients, today, Doctor?" After this show of complete confidence that the intern has seen his patients and taken a personal interest, the response will be prompt. A recital of important changes or any complications needing the physician's special care will be on the tip of his tongue. Or if all is well, he will say, "Mrs. so-and-so is doing beautifully. If you are in a hurry she need not be seen today."

While in medical school, the intern learned his clinical medicine at the feet of astute professors. Their diagnostic acumen and teaching finesse firmly implanted didactic facts in his mind. He knelt at their feet four long years, listening to the masters and longing to emulate their skill. On entering the hospital he realizes that much of his knowledge is theoretical. He is anxious to see and treat patients and to prove from experience — theory is fact. He looks appealingly to the visiting staff to be his teachers. His fire for knowledge, however, may be deplorably smothered by the cold-shouldering staff man, who assumes a "better-than-thou" attitude and treats him like something akin to a floor mat.

The doctor may appropriately take his superior place as clinical instructor. The intern is crying for teaching. He considers his internship worthwhile if an occasional chief drops a few pearls from the treasure chest of experience. And it is not beyond the realm of possibility that the junior will be able to reciprocate with a few kernels of gold — nuggets recently pocketed in medical school and facts that may be useful in practice. New therapeutics are fostered by interns and residents, as well as tried and proved by them.

In payment for instruction, the intern will dig through the cumulative index for some article that his chief would like and will abstract it for him. He will graciously spend hours in diligent search for the latest treatment of a patient with chronic arthritis.

Psychotherapy, if indulged at all, can devour the lion's share of any doctor's time. In fact, time is so limited on hospital rounds that such therapy is prohibitive. Either it is deleted from the patient's care or a psychologist is called in. Here the loyal intern can shine. It would be sheer naïveté to allow an intern to approach the nervous patient without previous introduction and instruction by the patient's family physician. But after such a status is attained, the "man in white" can render suave, persuasive psychotherapy by proxy for his chief. He can give patients encouragement and inspire confidence to hasten recovery and can thus save many hours of tedious tongue trilling, at the same time giving the patient an added service that not otherwise would have been received.

If a practice is a bit too large for one man to handle and a new man is needed, a fertile field from which to choose an aide comprises the young, red-blooded, hospital interns. And there is no better way to select one than to observe various interns in their care of patients. By permitting them the freedom an assistant enjoys, the staff man sees how responsibility is borne. In this way a partner may be chosen who clicks with colleague and patient. Meanwhile, the heavy burden of routine is lifted from the senior man's shoulders, his attention can be devoted to critical patients.

A pet peeve of the junior man in the operating room is the "eager beaver" surgeon — the one in such a mad rush to earn his first million dollars that he never allows the intern

to do anything but bold retractors or get out of his way. The surgeon believes that the preoperative and postoperative care of his patients is sometimes not just what it ought to be, perhaps there is a reason. If he permits the intern to consider himself an integral part of the surgical team, not ornament or a modified scrub nurse, he will soon note a remarkable improvement in the intern's interest in the postoperative course of patients.

Whenever the intern performs a procedure, minor though it be, he tacitly assumes that the patient is his own. He did something for the patient, therefore, he is obligated to care for his patient, and he is appreciative for the surgeon's generosity. He repays by close watch over postoperative patients. Menial chores are cheerfully performed, intravenous injections gladly given, dressings changed and wounds overserved with special care, since one of his own sutures may have gone into the bandiwork of that operation.

The intern does not ask for the surgeon's knife, but mere for an opportunity to learn a little surgical technique and the privilege to get the feel of things at the operating table. The chance of tying a few knots, snapping on hemostats, closing skin incisions and performing minor procedures under supervision. Such small gestures of confidence in the intern do take a little extra time on the part of the surgeon. But the time is well invested. It will pay big dividends in the care of surgical patients.

Small favors shown the intern not only will make for better intern training but also will simultaneously lighten the load of the staff doctor. The loyalty of the intern to his staff man and hospital will be reflected in more pleasant and more efficient hospital management. Most important, the patient will reap rich rewards in greatly improved hospital care and his esteem for doctor, intern and hospital will increase accordingly.

LIEUTENANT J. DE WITT FOX, M.C., A.U.

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Fort Sam Houston, Texas

INTRODUCTION OF DIGITALIS INTO NORTH AMERICA

To the Editor: A New Hampshire physician first used *Digitalis purpurea* in North America. Hall Jackson (1735-1797) lived in Portsmouth and was well known in New England. His father, Clement Jackson, was a doctor, and from him Hall received his early medical education. For three years he attended lectures in London at the public hospitals and made many friends there. At that time his principal interest was in smallpox. He returned to the colonies, and in 1766 he was called to Boston because of a smallpox epidemic. Later he opened a smallpox hospital on Hensell's Island. Five days after the Battle of Concord he offered his services in raising a company of Minute Men. On June 19, 1775, he was again summoned to Boston to take care of the wounded from the Battle of Bunker Hill, and he later became surgeon of a regiment that fought through the Ticonderoga Campaign. In November, 1775, he was appointed chief surgeon of all New Hampshire troops in the Continental Army, with the rank of colonel.

His interest in digitalis dated from the reading of William Withering's treatise, which he had received from London. Enthusiastic over the results that Withering had obtained, he sent to London for some of the powdered leaf and used it on his own patients. His results were so good that he wrote to Withering to tell him. Withering responded by sending him some of the seeds to be planted in New England. He suggested that the seeds be sent to other physicians in the state.

Jackson's first letter to Withering is now in possession of the Royal Society of Medicine, London, whose librarian, Miss G. F. Home, has kindly allowed its use in this note. It reads as follows:

Portsmouth, New Hampshire
North America
February 9, 1781

Sir,

Your inestimable treatise or account of the Fox glove and its medical uses, with practical remarks on dropsy, and other diseases, has found its way to this remote part of the globe. It must greatly add to the satisfaction that daily arises in your mind, on seeing so many

distressed fellow-mortals relieved by your personal advice, and administrations, to reflect that thousands at the most distant ends of the earth, are wishing to offer their tribute of gratitude for your indefatigable endeavours for the good of mankind

The gentlemen of the Society of Medical observations, and enquires, in London, the ingenious and worthy Doctors, Percival and White, of Manchester, with many others, of this day, in England, will never know how much the world is indebted to them for their publications, not only the present age, but generations yet unborn will bless their memory

There is no disorder more prevalent in this country than dropsy, our summers are extremely hot, our winters intensely cold, only two of the spring and fall months may be called temperate, our days in the winter are short, consequently our labouring people work but a few hours, the remainder of the time is spent in a sedentary, idle manner, and too often in an immoderate use of spirituous liquors. Our lumber trade to the West India Islands, returns in large quantities of rum and Molasses of the latter is distilled amongst us an inferior, cheap kind of rum, which is evidently unwholesome, it is generally used immediately from the still, it has an empyreumatic taste, and is wholly destitute of the mildness of rum that has undergone agitation at sea, and a few months age, a common labourer may receive five quarts of this new, strong, and fiery spirit, for a short day's work, from this plenty and cheapness the use is too general, and immoderate, and it is a just observation that those who indulge too freely in the use of spirits, are least anxious for substantial food. Their appetites are pallid, the solids weakened, the fluids irritated, and increased, obstructions formed, and dropsies become frequent. As yet no specific reason has been found, but in most cases, after a longer, or shorter time, the disease has proved mortal. Life in many cases has been prolonged to a considerable length of time by repeated tapping, but this has generally been with female subjects, where the disorder was of the encephaloid kind. Our remedies in general, have been such as are used in Europe, in like cases. The squills have been considered as the most powerful diuretic, and mostly depended upon, and some few have been relieved by their use, where resolution has been strong enough to preserve against the nauseating effects thereof

I have taken your treatise in my pocket for six weeks, I have shown it with the incomparable, accurate, and elegant drawing, to all my acquaintance within twenty miles, but no one can recollect of ever seeing any of its kind, in America, I am persuaded however, that it would arrive to sufficient maturity in this country, but attentive cultivation as our natural productions in general, are much the same as those of England, with this difference, the wood of our large trees is not so compact and hard, our fruit trees, nor the fruits, so large, smooth, as those of the same kind, in Great Britain, our plants and herbage in general are a degree, or two, inferior to those in England, planted in equal good soil, and cultivated with equal attention, chamomile will not flower in this country, tho' I have seen, in a very favourable season, a few scattered single-flowers, in a large hed. These remarks are from my own observations, having spent the year 1762 in England for the advantage of medical improvements

I have the honor of being acquainted with John Lane, Esq., Merchant in London, to him I have sent for a small invoice of medicines, I have directed a small quantity of *Fol. Digitalis Purp. Siccat.*, also some of the powder, and seeds, but I greatly fear they have not as yet become articles of the shops, in London, would I be so fortunate as to obtain (to the care of Mr Lane) thro' your influence, and direction, a small quantity of the genuine seed, the plant should be most attentively cultivated, most carefully prepared and as opportunity will not be wanting to administer it, the most accurate observations and remarks, on its operation, and effects, shall be noted, and if you will permit me the honor, shall be communicated to you, for any further satisfaction, or remarks, you may wish to make on this truly valuable discovery

And now Sir, I should be most painfully embarrassed for an apology in troubling a gentleman of your character with so lengthy, and uninteresting a letter, without the least personal knowledge, or the remotest introduction, was I not assured that where so much merit, and good-

ness obtains, an indulgent candour will not be wanting toward one who is sincerely desirous [sic] of doing all the possible good, in the narrow sphere in which providence has placed him, and hoped not altogether from those motives that too often actuate the generality of mankind

I am Sir (tho' unknown) with the utmost veneration of respect
Your most obliged, most obedient

HALL JACKSON

P S I have directed to be sent me two or three sets of your account of the Fox-glove, for the purpose of dispersing them. Also your *Scarlatina anginosa*, outlines of Mineralogy, and anticipate with great pleasure your proposed Botanical Arrangement. Hope it will be published before my directions are completed and sent out from London. The extremes of heat and cold in this country may be judged from the following

The Thermometer, Fahrenheits' scale stood as followeth

Portsmouth 1785	July 5th	83°
	15th	75°
	30th	80°
August from the 15th to 30th		80°
1786 January — 15 to 19		8° below 0

N B The Thermometer was placed in the open air, and the observations made at noon

The text of Withering's reply to Jackson's letter is not available, but Jackson quotes from it in a letter to Ezra Stiles, which appeared in the January, 1787, issue of *The American Museum* and reads as follows

Portsmouth, (N H) April 30, 1787

Sir,

In the year 1785, that justly celebrated botanist, Dr William Withering, physician to the general hospital in Birmingham, Great Britain, published a treatise on the *Digitalis Purpurea*, (Fox-glove) and its medical uses, with practical remarks on dropsies and other diseases. This valuable treatise came into my hands the same year, it contains more than a hundred and fifty cases of dropsies, many of them of the worse and most complicated kind, cured or relieved by this efficacious plant. I last year received from London, a small quantity of the dried leaves, and some of the same in powder. From repeated trials here, I am fully persuaded, that neither Dr Withering, nor his numerous correspondents, have exaggerated its salutary effects, it is, perhaps, the most powerful diuretic in nature, and possesses a remarkable quality of abating the acceleration of the heart, and retarding the circulation of the blood

By the last ship from London, and last post from Boston, I was honoured with a very polite, obliging, and interesting letter from Dr Withering, and favoured also with a quantity of seeds of the Fox-glove by him. He writes, "I send more that you will distribute them into other states"

It is with much pleasure that I comply with the doctor's humane wish, in enclosing you a small quantity of them, being fully persuaded you will find equal satisfaction in the cultivation of so useful and ornamental a vegetable, it bears a beautiful purple bell-flower, worthy a place in any garden

I take liberty of transcribing two other passages in the doctor's letter, which, I think, may, with propriety, accompany the seed. "I am more and more convinced, that the *Digitalis*, under a judicious management, is one of the mildest and fastest medicines we have, and one of the most efficacious. I believe it is not necessary to create a nausea or any other disturbance in the system. I never use more than 1 scruple *fol suc* $\frac{1}{2}$ lb of infusion, and in substance rarely more than 3 grains in twenty-four hours"

"*Digitalis* has cured two other cases of insanity in this neighborhood, and three cases of *hemoptoe*, the latter were of a kind attended with a quick bounding pulse, and I directed the medicine, from the quality I knew it possesses of abating the actions of the heart"

I would just mention, that it is a biennial plant, and I conclude it will take some little care to preserve the roots from the severity of the frosts in this cold climate, though it flourishes spontaneously in the fields of England

My good intention must be my apology in the liberty I have taken in troubling a gentleman of your character with so lengthy a letter, altogether professional. I wish to promulgate so valuable an acquisition in medicine, and am so unfortunate as not to be acquainted with any gentlemen of the faculty in your state.

I am, Sir, etc

HALL JACKSON

The Rev Ezra Stiles, president of Yale College

DOUGLAS CARROLL, M.D.

Johns Hopkins Hospital
Baltimore 5

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Essentials of Clinical Allergy By Samuel J. Taub, M.D., professor of medicine, Cook County Graduate School of Medicine, and attending physician in medicine, Cook County Hospital. 8°, cloth, 198 pp., with 16 plates, 2 figures and tables. Baltimore: The Williams and Wilkins Company, 1945. \$3.00.

This manual is written for the general practitioner and medical student. The author has attempted to present a practical clinical approach to the various allergic diseases, as seen in practice. Theoretical discussions have been avoided, and the importance of a broad knowledge of internal medicine is emphasized for the better understanding of allergic conditions. Considerable space is devoted to the discussion of seasonal and perennial hay fever and asthma and to skin disturbances due to allergy. Valuable tables of the pollen flora and pollination dates and skin tests are included in the text. The illustrations of pollen and pollen plants should prove valuable. The final chapter describes various special diets and recipes. This manual should prove of value to the practicing physician.

A Handbook for Dissectors By J. C. Boileau Grant, F.R.C.S., Ed., M.B., Ch.B., professor of anatomy, University of Toronto, and H. A. Cates, associate professor of anatomy, University of Toronto. Second edition. 12°, cloth, 390 pp. Baltimore: The Williams and Wilkins Company, 1945. \$2.50.

The first edition of this manual was written for use in conjunction with *A Method of Anatomy* by the same author. In this edition the handbook has been separated from the latter, all the references to the larger work have been deleted, and instruction for the dissection of every region has been included. The account of the brain is written to meet the needs of the beginner, for whom it should be sufficient. The handbook is designed as an inexpensive guide that students can use without much concern for its ultimate condition but that contains enough information for the identification of any structure met with in the dissection room. It should prove valuable for this purpose.

NOTICES

ANNOUNCEMENTS

Dr. Harry Blotner announces the removal of his office from 189 Bay State Road to 419 Commonwealth Avenue, Boston.

Dr. Joseph Lentune announces the removal of his office from 520 Commonwealth Avenue to 395 Commonwealth Avenue, Boston.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, December 3, at 8:15 p.m. Dr. Shields Warren will speak on the subject "Medical Aspects of the Bikini Experiments." This will be followed by a discussion from the floor.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular meeting of the New England Dermatological Society will be held in the Skin Out-Patient Department of the Boston City Hospital on Wednesday, December 4, 2:00 p.m.

JOSEPH H. PRATT
DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, December 4 — Infections Due to *Bacillus Pyocyaneus* (*P. aeruginosa*) Treatment with Streptomycin. Dr. Malcolm Stanley.

Friday, December 6 — The Present Status of the Peptic Ulcer. Dr. Sara M. Jordan.

Wednesday, December 11 — Xanthomatous Biliary Cirrhosis. Drs. S. J. Thannhauser and H. E. MacMahon.

Friday, December 13 — The Plastic Repair of Burn Wounds. Dr. Malvin F. White.

Wednesday, December 18 — Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon.

Friday, December 20 — Roentgenology in the Study of Heart Disease. Dr. Merrill Sosman.

On Tuesday and Thursday mornings, Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek. Medical rounds are conducted each weekday by members of the staff from 12:00 to 1:00 in the Lecture Hall.

All exercises are open to the medical profession.

Conferences will be discontinued December 24, 1946 through January 11, 1947.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, DECEMBER 5

FRIDAY, DECEMBER 6

*9:00-10:00 a.m. The Present Status of the Peptic Ulcer. Dr. Sara M. Jordan. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.-12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

MONDAY, DECEMBER 9

*12:15-1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

TUESDAY, DECEMBER 10

*12:15-1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*8:00 p.m. Harvard Medical Society Amphitheater, Peter Bent Brigham Hospital.

WEDNESDAY, DECEMBER 11

*9:00-10:00 a.m. Xanthomatous Biliary Cirrhosis. Drs. S. J. Thannhauser and H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*11:00 a.m.-12:00 m. Medical Clinic Amphitheater, Children's Hospital.

*12:00 m. Clinicopathological Conference (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital.

*2:00-3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services Amphitheater, Children's Hospital.

*7:15 p.m. Graduate Seminar in Pediatrics. Children's Medical Service, Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

OCTOBER 11-MAY 14. Metropolitan State Hospital. Page 398, issue of September 12.

OCTOBER 15-DECEMBER 5. Exhibition to Commemorate of Ether Centenary. Page 570, issue of October 10.

DECEMBER 3. Greater Boston Medical Society. Notice above.

DECEMBER 4. New England Dermatological Society. Notice above.

DECEMBER 4-20. Joseph H. Pratt Diagnostic Hospital. Medical Conference Program. Notice above.

DECEMBER 5. Suffolk Censors meeting. Page 346, issue of September 5.

DECEMBER 7-12. American Academy of Dermatology and Syphilology. Page 570, issue of October 10.

DECEMBER 12. Headaches from the Ophthalmological Standpoint. Dr. Edwin B. Dunphy. Pequotuck Association of Physicians. 8:30 p.m. Haverhill.

DECEMBER 18. New England Society of Physical Medicine. Page six, issue of November 21.

(Notices continued on page xxx)

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PRESENT TRENDS IN OBSTETRICS*

S A COSGROVE, M.D.†

JERSEY CITY, NEW JERSEY

THE obstetrician finds his efforts in behalf of pregnant and parturient women consisting of the prevention and alleviation of four great menaces. These are pain, hemorrhage, toxemia and sepsis. The significant trends in practice, therefore, are perhaps best dealt with as pertaining to these subjects.

PAIN

Until a comparatively recent epoch in medical history, pain was considered the inevitable and inescapable lot of child-bearing women. For the past hundred years, however, the search for a method of alleviating the pain of labor has been continuous and assiduous, men have long hoped for the means of making labor completely painless. From time to time it has mistakenly been believed that this ideal objective had actually been accomplished. The procedures devised periodically in this high hope have successively been found to involve such dangers, either for the mother or the baby, as to render their applicability seriously limited. For practical purposes, the means of relieving pain may be divided into two groups.

Analgesic Agents

The first group embraces drugs that make more tolerable the pains of the tedious first stage of labor and a portion of the second stage. They comprise agents truly analgesic in their potentiality, such as morphine, and those that are merely amnesic, obliterating the patient's subsequent recollection of suffering. Agents of these two groups are frequently combined. The number of such agents is large. The most venerable in length of use are opium and its derivatives, such as morphine and heroin. One of the most recent is Demerol, a synthetic preparation quite like morphine in some of its important pharmacologic characteristics.

The danger that principally limits the use of such agents is the marked tendency of all of them to narcotize the fetus and to make for delay and sometimes failure in the establishment of normal respira-

tion after birth. In these respects Demerol, which has had a fairly extensive but perhaps not thoroughly adequate clinical trial in many hands, appears to be the least dangerous.

Another group of drugs having a powerful soporific action combined with a modicum of analgesic and amnesic properties comprises the barbiturates, of which many varieties have appeared. These preparations vary in the promptness, power and duration of their action. For this reason, some attempt has been made to individualize patients in the selection of the particular barbiturate deemed best suited for the situations under which it is administered.

Evidence is accumulating that the most popular agents used a few years ago for the relief of first-stage pain — the so-called "basal analgesics," are far from innocuous, particularly in their effect on the fetus. Increasing recognition of this fact is tending to make them somewhat less popular, but their use is still extensive, and in my opinion they have a distinct place in the resource of the obstetrician.

The only drug whose usefulness depends directly and wholly on its amnesic powers is scopolamine, although several of the others mentioned above have this property in some degree. A few practitioners, appreciating the dangers of the opiates and apparently convinced that the subsequent effect on the parturient patient's psyche in her recollection of an exceedingly painful experience is the most important factor to overcome, have depended largely or solely on the administration of scopolamine for this purpose. The majority of practitioners, however, prefer actually to abolish pain so far as it can safely be done. These men therefore use scopolamine, if at all, only as an adjuvant to other more definitely pain-relieving drugs. Scopolamine is often thus combined with many of the agents already named. It must not be forgotten that scopolamine is derived from one of a dangerously poisonous group of plants. Occasional idiosyncrasy or carelessness in dosage may result in disaster.

Anesthetic Agents

The second group of pain-relieving agents is applied in the management of the terminal phase of

*Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 13, 1946.
†Clinical professor of obstetrics, Columbia University College of Physicians and Surgeons; assistant medical director, Hudson County and Jersey City hospitals; medical director and superintendent, Margaret Hague Maternity Hospital.

the second stage of labor, characterized by the actual extrusion of the fetus through the vaginal introitus. They are used for more complete and definitive anesthesia against the excruciating pain characterizing this part of labor.

Again the variety of these agents is large. They fall into two distinct and different groups.

The first includes those that act on the brain itself, abolishing pain by narcotizing the entire cerebral sensorium. They are most frequently administered by inhalation, entering the blood stream through the lungs and exerting their physiologic effect on the brain through the blood.

Ever since Simpson, almost a century ago, taking his cue from the first historic surgical use of sulfuric ether, in this very city, applied this agent and subsequently chloroform to the relief of pain in parturition, each one of the many agents devised for inhalation anesthesia for any purpose has been applied to obstetric practice.

Ether, oldest of them all, still retains an important place in the obstetric armamentarium, especially in practice outside hospitals and even in hospitals where the service of expert anesthetists in the administration of other agents is not available. Ether has also been extensively used in the past, and continues to be somewhat used as a labor analgesic, as well as a terminal labor anesthetic, administered in oil by rectum by the well known but now somewhat archaic Gwathmey technic.

Chloroform, used soon after ether and preferred by Simpson, shortly became much the most important obstetric anesthetic and served several generations of physicians well. For the last quarter century it has lost this pre-eminence. It has been accused of a high mortality rate for mothers and of dangerous toxic side-effects, particularly in the liver. It has almost completely dropped out of use in most leading American clinics. I am not sure, however, that it justly deserves the total oblivion into which it has fallen. I suspect that it continues to serve well many physicians practicing outside hospitals, who appreciate its flexibility and would not willingly forego the help that it constantly affords. I am old enough to remember well my own debt to chloroform for service rendered in the past.

Perhaps foremost in hospital use today for the termination of labor by inhalation anesthesia is nitrous oxide, administered with appropriate proportions of oxygen, in an apparatus specially designed for this use. It is reasonably safe. It must be emphasized, however, that its safety is only relative and that it may be exceedingly dangerous in untrained hands. Cyclopropane, ethylene and vinyl ether are to some extent employed.

All these agents, acting centrally on the maternal brain, have the tremendous disadvantage that they also act centrally on the fetal brain. One cannot narcotize the mother by means of them without a

fairly corresponding degree of narcotization of the fetus. Therein lies a serious restriction of their usefulness. Moreover, I have been impressed by the heightened danger represented by the use of the narcotic agents in the fact of their synergism with other agents, particularly opium derivatives, that are frequently included in the regime of balanced analgesia prior to the administration of the inhalation narcotic. Such synergism represents a real jeopardy to the fetus from damaging or fatal asphyxiation.

The other group of agents available for the termination of the second stage of labor, as well as participating to a certain extent in the program of the earlier stages, are applied only to the peripheral neuron of the mother's nervous system. They do not enter the blood stream. They do not affect the general sensorium of the mother, or the cerebral and vital centers. In their entire innocuousness so far as the fetus is concerned, they present tremendous advantages over agents that depend on narcotization of the whole nervous system of the mother. The most widely used agent of this group is novocain. Metycaine, pontocaine and other agents have been similarly employed. Novocain, by its relatively low toxicity, remains probably the standard for this type of anesthesia. These agents are administered by so-called "conduction anesthesia," in which the drug is brought into contact with the peripheral nerves at some point distal to their exit from the spinal cord.

The most immediate and complete of such methods is spinal or intrathecal anesthesia, in which a solution of the anesthetic agent is injected into the thecal sac surrounding the spinal cord at points below the termination of the cord itself, anesthetizing the nerve roots springing from the cord a short distance away from their origin. Another is caudal anesthesia, in which solutions of the anesthetic agent are injected into the spinal canal external to the thecal sac, through the hiatus of the sacrum, exerting their anesthetic effect on the nerve roots as they traverse that space or immediately beyond it where the neurolemma ends. Thirdly, the anesthetic agent may be so injected as to bathe specific principal nerve trunks in continuity, as in parasacral injection. Finally, local infiltration, frequently combined with conduction anesthesia of a few important nerve trunks, may be employed.

These methods of anesthesia, applied to the peripheral nerve segment, are taking an increasing place in obstetric practice. This is regarded as a constructive tendency because of the vast advantage to the fetus embodied in these methods as compared to those that specifically poison the brain through the blood stream.

These procedures also have many points of advantage so far as the welfare of the mother is concerned, particularly when the mother is handicapped by certain intercurrent diseases either more or less

specific for pregnancy or not depending directly on the fact of pregnancy. Each has its own advantages and disadvantages.

I have employed spinal anesthesia in obstetrics for twenty years. There has been and continues to be much criticism of its obstetric use from the standpoint of danger of sudden death. From an experience of many thousands of cases, however, I believe that it constitutes an ideal method for vaginal delivery, in which it can be used in small enough dosage to eliminate this danger and in which I have observed no other important unpleasant sequelae. I have also used spinal anesthesia extensively for obstetric laparotomies, with a low mortality. In consideration of the handicaps presented by the patients who have succumbed, however, I am not impressed with the probability that any other method of anesthesia in those particular cases would have been significantly less dangerous.

My experience has been with the so-called "one-shot" or single-injection method. Continuous spinal anesthesia, in which successive small doses are administered through a needle left in situ, has recently had increasing use. In spite of the bitter and, in my opinion, at times strongly biased and unjust criticism of spinal anesthesia, there is no doubt that it is being more and more widely used.

Caudal anesthesia, a method by no means new, was brought sharply to the attention of the obstetric world about five years ago by Hingson, an honest and well qualified anesthetist in the United States Public Health Service, in the form of continuous caudal anesthesia. The first reports were undoubtedly overenthusiastic. Hingson apparently thought that he had actually achieved in this method an almost universally applicable approach to the obstetrician's dream of painless labor. This belief was shortly disappointed. With increasing experience, he recognized and defined a number of limitations and dangers that reduced the method to one not applicable in the vast majority of cases from the initiation of labor pains or for an unlimited time after the inauguration of the anesthesia. From time to time he has honestly re-evaluated the indications and contraindications, as well as the advantages and disadvantages, of the method.

At the present time it seems that caudal anesthesia is not, in any but the most expert hands, properly applicable in more than one out of four or five patients or for a total period longer than six to eight hours. Distinct dangers inhere in the method, avoidable only by the most meticulously expert technic. This fact makes it essential that the procedure be used only by physicians and nurses especially trained in this technic. It requires in each case the constant close attention during the whole period of anesthesia of either the responsible obstetrician or another physician, such as an especially trained anesthetist. This necessarily limits the number of patients who can derive the benefit

of this method. It is obvious that, except in large teaching hospitals where caudal anesthesia can be afforded to patients only on the basis of its educational value, the necessarily high cost entailed by the close attention of highly qualified physicians is beyond the capacity of the majority of patients.

The most obvious dangers of caudal anesthesia are the inadvertent injection of the anesthetic solution into the thecal sac, the injection of the solution directly into the blood stream and, of course, the rare but ever present danger of infection of the meninges. Other technical dangers are recognized. The anesthesia is neither so prompt nor so uniform as spinal anesthesia, the dangers are of the same nature and the difficulty and the cost are greater.

Results in successful cases are most satisfactory, and many a woman has been deservedly grateful for the relief of suffering afforded. The procedure is not, however, and can never be the universal panacea that it was originally hoped to be. It is a resource that the well qualified obstetrician should consider at his command, but it is incapable of supplanting other methods in the majority of cases.

Infiltration anesthesia, with or without peripheral nerve block, is the safest of all anesthetic methods. Some of its proponents claim that there has never been a fatality justifiably attributable to it. This is probably such an exaggeration as the use of the word "never" almost always implies in medicine. The procedure is not universally applicable, since neurotic patients are not favorable subjects, and unbiased observers are not infrequently impressed with its lack of complete efficiency. A modicum of special training and adept technic and sometimes a high degree of patience and tolerance on the part of both the operator and the patient are required. There is undoubtedly, however, a steadily increasing use of this method, and since the possibility of death or serious accident is almost completely negligible, this trend is indeed salutary.

HEMORRHAGE

The reduction of the danger of hemorrhage, which is actually the most frequent of the purely obstetric causes of puerperal death, continues along lines long since laid down. They include the following: better training in exact and early recognition of ectopic gestation, placenta previa and abruption of the placenta, less reliance on the outmoded packing of the uterus, a more intelligent search for the sources of bleeding in the various parts of the parturient canal and uterus, and the application of more definitive operative therapy to several of these sources when demonstrated, increasing knowledge and appreciation of the significance of Rh-factor incompatibility, not only concerning the health and survival of the fetus, but also regarding the dangers of an unfavorable transfusion reaction in the mother, and the inclusion of blood-group and Rh-

the second stage of labor, characterized by the actual extrusion of the fetus through the vaginal introitus. They are used for more complete and definitive anesthesia against the excruciating pain characterizing this part of labor.

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All these agents, acting centrally on the maternal brain, have the tremendous disadvantage that they also act centrally on the fetal brain. One cannot narcotize the mother by means of them without a

fairly corresponding degree of narcotization of fetus. Therein lies a serious restriction of their usefulness. Moreover, I have been impressed by heightened danger represented by the use of the narcotic agents in the fact of their synergism with other agents, particularly opium derivatives, that are frequently included in the regime of buprenorphine analgesia prior to the administration of the inhalation narcotic. Such synergism represents a real jeopardy to the fetus from damaging or fatal asphyxiation.

The other group of agents available for the termination of the second stage of labor, as well as participating to a certain extent in the program of the earlier stages, are applied only to the peripheral neuron of the mother's nervous system. They do not enter the blood stream. They do not affect the general sensorium of the mother, or the cerebral and vital centers. In their entire innocuousness as far as the fetus is concerned, they present tremendous advantages over agents that depend on narcotization of the whole nervous system of the mother. The most widely used agent of this group is novocain. Metycaine, pontocaine and other agents have been similarly employed. Novocain, by its relatively low toxicity, remains probably the standard for this type of anesthesia. These agents are administered by so-called "conduction anesthesia," in which the drug is brought into contact with the peripheral nerves at some point distal to their exit from the spinal cord.

The most immediate and complete of such methods is spinal or intrathecal anesthesia, in which a solution of the anesthetic agent is injected into the thecal sac surrounding the spinal cord at points below the termination of the cord itself, anesthetizing the nerve roots springing from the cord a short distance away from their origin. Another is caudal anesthesia, in which solutions of the anesthetic agent are injected into the spinal canal external to the thecal sac, through the hiatus of the sacrum, exerting their anesthetic effect on the nerve roots as they traverse that space or immediately beyond it where the neurolemma ends. Thirdly, the anesthetic agent may be so injected as to bathe the specific principal nerve trunks in continuity, as in parasacral injection. Finally, local infiltration, frequently combined with conduction anesthesia of a few important nerve trunks may be employed.

These methods of anesthesia, applied to the peripheral nerve segment, are taking an increasing place in obstetric practice. This is regarded as a constructive tendency because of the vast advantage to the fetus embodied in these methods as compared to those that specifically poison the brain through the blood stream.

These procedures also have many points of advantage so far as the welfare of the mother is concerned, particularly when the mother is handicapped by certain intercurrent diseases either more or less

prompt and adequate treatment and timely termination of pregnancy in toxemia applies with special emphasis in the hypertensive patient with superimposed toxemia

SEPSIS

The availability of the sulfonamides and of several antibiotic agents of high efficiency has greatly increased the resources of the obstetrician in treating the septic complications of pregnancy, labor and puerperium

Streptomycin, not yet generally available, appears to promise great value in certain infections not amenable to other antibiotics. It is to be hoped that it may presently be released on a commercial scale and that similar agents may be forthcoming

It must be cautioned, however, that these valuable agents are not universally efficacious, even when culture studies appear to indicate them specifically. They must not be depended on to replace, or justify carelessness in, the surgical technics necessary and efficacious in preventing sepsis. The use of these agents in a prophylactic sense, or on a tentative basis lacking knowledge of specific bacteriologic indications, is debatable, but the uncertainty of bacteriologic findings and the loss of time in determining them appear to justify such practice.

The increasing recognition of the value of rather small, frequently repeated blood transfusions in the treatment of infective complications is wholly constructive. This method is occasionally limited by unfavorable reactions, however. Especially meticulous care is necessary in grouping and cross-matching

The present interest, amounting perhaps to a craze, in the surgical treatment of thrombophlebitis and phlebothrombosis on the part of many surgeons is believed to have little support from the obstetrician. The rarity of puerperal death from embolism, the efficacy of other methods of treatment and the sometimes long-lasting serious sequelae of surgery seem to justify this attitude

* * *

Finally, it is believed that there is a continuing and increasing trend toward what Dr Willard Cooke, of the University of Texas, calls "rationalism" in obstetrics. This is considered a better term than "conservatism" or "radicalism," which are hard to define and often interchangeable. Perhaps the wish is father to the thought that this trend is wholly desirable. Rationalism includes such objectives as Bingham's fine phrase, "Keep the normal obstetric case normal," and the principle that medical and surgical complications of pregnancy should be appropriately medically and surgically treated, without interference with pregnancy. It does not embrace, on the one hand, blind confidence that pregnancy always is and will remain physiologic, or on the other, a baseless fear that pregnancy may not be successfully managed in the presence of almost any complication. Intelligent improvement in obstetric practice will be principally predicated on thoughtful individualization of cases on the basis of such rationalism

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factor determination as a routine part of early prenatal care.

A further vital step in combating hemorrhage is increasing provision and improvement in the operation of blood and plasma banks. A recent temporary augmentation of the resources of hospitals in this respect has been the release to them, through state agencies, of large amounts of dried plasma originally provided for the armed forces. Frequent difficulty in obtaining compatible blood from the standpoint of both blood-grouping and Rh-factor compatibility is being lessened by technical improvements in the preparation and storing of blood.

The work of Dr. Diamond, of Boston, in such improvement is significant. The artificial neutralization of the A and B agglutinins permits the pooling of blood compatible for all recipients so far as the basic blood groups are concerned. Such pooled blood may then be divided into two pools, depending on its Rh-factor characteristics. Selection of bloods for individual recipients then depends only on the Rh characteristics of the recipients.

It is entirely possible that the more widespread determination of the titer of Rh antigens in Rh-recipients may further simplify this problem. The whole effect of these technical improvements, of course, is to save time in the administration of blood under circumstances in which time is a highly important consideration.

The blind unreasoning dependence on the antepartum administration of vitamin K that apparently possessed so many members of the profession only recently is being replaced, on the basis of objective studies of its results, by a saner realization of the limitations of this therapy. Thus, the naïve statement heard not too long ago in one of the leading special societies, "We shall not worry about post-partum hemorrhage in the mother, for, of course, she has received vitamin K before labor," is now recognized for its manifest absurdity. Even the efficacy of this agent in reducing infant mortality, either from hemorrhagic disease of the newborn or from bleeding on a traumatic basis, is open to serious question.

These facts do not negate the present probable wisdom of using vitamin K in post-partum uterine inertia or in infants suspected of suffering from actual or potential hemorrhage. But it is only a possibly useful drug, not a miraculous substitute for other time-tried methods.

TOXEMIA

It cannot be said that there has been any significant advance in the knowledge of the pathogenesis of toxemia, in more satisfactory classification or in methods of treatment whose objectives are fairly well standardized in spite of a wide variety of detail in the methods themselves. Nor is there any true prophylaxis for toxemia except that embodied in early institution and intensive

performance of prenatal supervision. Meticulous attention to all the details of hygiene, proper diet and vitamin balance should be embodied in the program.

Clearer concepts of the necessary treatment of the toxemias, however, are emerging. The objectives of such treatment are conservation of maternal life from immediate hazard, conservation of fetal life and conservation of maternal health and long-range survival. The primary requisites to accomplish the objectives in the highest degree are early recognition of toxemia by presumptive and slight clinical evidence, prompt institution of the fullest regimen for control of the disease when discovered and definite—if necessary, radical—control of the time the disease is permitted to persist.

There is no degree of toxemia that is clinically negligible. Even occult edema suggested by any exorbitant weight gain should be considered, and treatment at once begun. More definite indications, even in only slight degree, require the fullest program of treatment, generally including hospitalization. Fulmination of severe toxemia is not always presaged by orderly progression from mild through recognizably severer forms. In a high percentage of cases eclampsia supervenes directly on pre-eclampsia of the supposedly mild type.

The only definitive treatment of any form of toxemia is termination of pregnancy. As already pointed out, all the objectives of treatment depend for success on limiting the time that the toxemia is allowed to persist. Time of interrupting the pregnancy is therefore of utmost importance. This time necessity often warrants radical means in preference to less certain and protracted methods. Cesarean section is sometimes appropriate on this basis alone. Such termination of pregnancy is surely salutary in reducing immediate maternal risk and has unmistakably been shown to be equally valuable so far as the mother's subsequent health and life expectancy are concerned. It is not inimical (at least after the thirty-fourth week) to the baby's chances of survival—the single hazard of prematurity is merely substituted for the many dangers from abortion, suboxidation, malnutrition and perhaps direct toxicity.

The single form of toxemia in which the foregoing considerations are not true is eclampsia, in which the seriousness of the clinical picture necessitates entire concentration on the medical treatment of the mother. The baby's interest must be subordinated to hers. Abundant evidence proves that only rarely and under certain special conditions is the eclamptic mother's interest served by deliberate interruption of pregnancy.

Pre-existing hypertension represents only a moderate immediate hazard to the pregnant patient and the fetus, and virtually no remote hazard, provided superadded toxemia does not occur. Hence, all that has been said about the early recognition,

point is the appearance of bile-stained urine, which is frequently observed by the patient before jaundice develops.

The icteric phase averages two to four weeks, and when jaundice appears fever subsides and the gastrointestinal complaints are apt to become prominent. Anorexia, which is peculiarly severe, nausea and less often vomiting, epigastric discomfort and pain in the region of the liver — especially on jarring, bending, rolling on the right side in bed and sometimes on coughing and deep breathing — are frequent and significant complaints. On careful examination the liver is often found to be enlarged and tender, and the spleen may be palpable. Jaundice as a general rule reaches a peak in about a week and begins to fade fairly rapidly. Soon after jaundice appears there is usually a remarkable amelioration of complaints, return of appetite and disappearance of the feeling of malaise. Abdominal discomfort, lassitude and other symptoms may persist, but liver tenderness tends to subside and the liver gradually returns to normal size.

In some cases icterus becomes progressively worse, a marked fetor hepaticus is noted²⁵ and the patient becomes restless, irritable and delirious. Coma, often with hemorrhagic manifestations, develops, and death from acute hepatic necrosis ensues.

The convalescent phase, defined as the period following clearance of the jaundice and cessation of all signs of active disease, usually lasts about seven to fourteen days. Barker and his associates²²⁻²⁴ have clearly pointed out that proper evaluation of recovery, especially regarding toleration of activity, is essential if relapse and chronic hepatitis are to be avoided.

DIAGNOSIS

Except in the presence of an epidemic, preicteric cases and those without icterus are not likely to be recognized in civilian practice. From the diagnostic standpoint, a history of association with jaundiced persons or the administration of blood, plasma, serum and parenteral fluids is of great importance. Clinical findings — especially severe anorexia and nausea, tenderness over the liver and bile-stained urine — are also of particular significance.

In civilian as in military life, jaundice in young people usually offers few diagnostic problems. Sporadic cases of infective hepatitis in civilian life, however, may present serious diagnostic difficulties. White,²⁷⁻²⁹ discussing diagnostic problems in the presence of jaundice, emphasizes the fact that infective hepatitis can occur at any age, in his series of 500 cases of jaundice, there were 101 patients with acute infective hepatitis, 60 per cent of whom were over thirty years of age. In an older and more heterogeneous group, greater possibilities exist for the occurrence of obstructive

jaundice due to biliary-tract disease and cancer. In addition, the various toxic, chemical and nutritional factors causing hepatitis and cirrhosis are more frequently encountered.

In an analysis of a personal series of 206 cases of jaundice in civilian practice, there were 82 cases of obstructive jaundice due to biliary-tract disease and cancer, and various forms of hepatitis and cirrhosis accounted for 124 cases, 42 of which were infective hepatitis. In 6 patients jaundice followed the administration of blood and plasma, 4 patients had associated with other jaundiced persons, and 32 cases were sporadic. In the 32 sporadic cases, 20 patients were over thirty-five years of age, and all but 1 of the severe cases and the 3 fatal cases occurred in patients over forty years of age. This agrees with the rather general impression that older patients do not stand liver damage so well as younger people, and Jones²⁹ points this out in association with chemical liver intoxication.

The most serious and practical problem in the treatment of the jaundiced patient is to decide whether the case is a medical or a surgical one.^{27, 28, 30} On the one hand, surgical intervention may save a life, whereas on the other, ill advised exploration may precipitate liver failure and death. The differential diagnosis between hepatitis and extrahepatic obstruction due to common-duct stone or cancer rests fundamentally on a careful evaluation of the history and clinical aspects of the case. Of special diagnostic value are such factors as the mode of onset, the degree, duration and course of the jaundice, the presence, character and location of pain, the occurrence of anorexia and nausea, the size, character and tenderness of the liver and the presence of an enlarged and nontender gall bladder or a palpable spleen. It has become increasingly evident that jaundice due to obstruction is not a surgical emergency and that proper preparation of the patient and evaluation of liver function have greatly reduced the mortality of operative procedures on the biliary tree. This increased period of observation, which has also allowed time for further study, constitutes in itself an important factor in limiting diagnostic errors.

Clinically and from the laboratory standpoint, acute infective hepatitis and that due to various chemicals, drugs and bacterial toxins closely resemble each other.³¹ Differentiation is usually difficult and in some cases impossible unless there is evidence of exposure to the hepatotoxic factor. Fortunately, chemical injury to the liver is infrequent as a general clinical problem, and the same principles of management can be applied to almost all forms of hepatocellular damage.

A great deal has been written concerning the role of laboratory tests in diseases of the liver and the extrahepatic biliary tracts.³²⁻³⁵ Although in themselves not diagnostic, a group of relatively simple procedures, carried out repeatedly, contribute in-

THE DIAGNOSIS AND TREATMENT OF INFECTIVE HEPATITIS*

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INFECTIVE hepatitis has been known chiefly as a disease of war, but it has been described frequently during the past three decades as a sporadic, endemic and epidemic disease occurring in civilian populations all over the world.¹⁻⁴ During World War II an unprecedented pandemic of infective hepatitis occurred, and the increasing prevalence of this serious disorder in civilian practice makes it imperative to utilize the newer concepts of the disease and to apply the knowledge and experience gained during the recent conflict to the best diagnostic and therapeutic advantage.

It is impossible, in the present state of knowledge, to designate the disease by an accurate nomenclature, in this paper infective hepatitis is used as a general term to include the sporadic and epidemic form (infectious hepatitis) and the parenterally transmitted disorder (homologous serum hepatitis). In view of the modern concept of the pathology of the disease, the term "catarrhal jaundice" should be discarded, not only because it is well established that many cases of infective hepatitis occur without jaundice but also because catarrhal jaundice has become synonymous with a benign and self-limited process, whereas there is increasing evidence that infective hepatitis is a serious and often treacherous disease.⁵⁻⁷

GENERAL CONSIDERATIONS

In spite of the vast amount of material available and the intensive studies carried out in this country and abroad, knowledge concerning infective hepatitis is still deficient, especially in the etiologic and immunologic aspects of the disease. In recent papers Janeway⁸ and Paul⁹ point out that the etiologic agent of infective hepatitis has never been seen, cultured or transmitted to laboratory animals. Since the agent passes through bacteria-tight filters, it has been considered to be a virus. It is stable, resisting heating to 56°C for at least thirty minutes, and withstands drying, freezing and the ordinary antibacterial preservatives. By means of experimental transfer in men, it has been shown that in the preicteric and early icteric stages of epidemic hepatitis the feces and blood contain the infective agent.^{9, 10} The blood of patients with serum hepatitis, in the incubation period and early icteric phase, has reproduced the disease in human volunteers when given by mouth and parenterally.¹¹⁻¹³ There are also reports on the infectivity

of urine and nasopharyngeal secretions, but the studies await further confirmation.^{9, 14}

Biopsy and autopsy material indicates that the essential pathologic process is a degeneration and necrosis of parenchymatous liver cells, with an inflammatory reaction and cellular infiltration in the portal spaces and sinusoids.^{15, 16} Usually, complete regeneration occurs, but fibrotic changes occur in classic cirrhosis have been described by Dible and others.¹⁷ Fatal cases present the picture of acute or subacute yellow atrophy of the liver.

Most investigators believe that serum hepatitis and epidemic hepatitis cannot be differentiated pathologically or clinically.¹⁸ Paul⁹ and Janeway, however, state that there are important differences such as a lack of cross immunity and the fact that the infective agent is present in the stools of patients with epidemic hepatitis and absent in those of patients with serum hepatitis. Epidemic hepatitis is often spread by contact, serum hepatitis rarely transferred in this fashion. Gamma globulin seems to be protective against the epidemic form but has apparently been ineffective to date in the prevention of serum hepatitis.¹⁹ From recent reports it is also noteworthy that the mortality of serum hepatitis is much higher than that in the epidemic type.^{5, 20, 21}

At present it is not clear whether these forms of hepatitis are caused by the same virus, by different or attenuated strains of the same virus or by different etiologic agents producing a similar clinical entity.

CLINICAL ASPECTS

Excellent and detailed descriptions of the clinical features of infective hepatitis have appeared in the literature.^{22, 23} The disease typically has preicteric, icteric and convalescent stages, although some patients have jaundice as the initial complaint and in others icterus may not develop—the *sine icterus* group.²⁴

The preicteric phase is usually of five to seven days' duration, and there is frequently an acute febrile onset accompanied by a chilly feeling, headache, malaise, weakness, generalized aches and pains, anorexia, nausea and occasionally vomiting. Sporadic cases encountered in civilian practice may have an afebrile and insidious onset, resembling in this respect many cases of serum hepatitis.

Physical signs are few, hepatic tenderness may be present, but enlargement and tenderness of the liver are likelier to occur just before or with the onset of jaundice. A most important diagnostic

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containing unsaturated fatty acids, have been limited in the diet, but Hoagland⁵³ has recently questioned the wisdom of this practice. Until further clinical and experimental data are available, a diet consisting of 350 to 500 gm. of carbohydrate, 150 gm. of protein and 50 gm. of fat may be considered adequate. Protein may be increased by the addition of supplementary feedings of methionine—substances rich in casein, such as cottage cheese, skimmed milk and various protein concentrates. When necessary, in vomiting or extremely sick patients, parenteral glucose, plasma, whole blood and purified human albumin⁵ may be utilized. Since the effect of the administration of parenteral amino acids on the liver in acute infective hepatitis is still under investigation and since a few untoward reactions have been reported, the use of these products should await further study.⁵⁴

The specific therapeutic indications and the exact dosage of vitamins necessary in acute infective hepatitis are unknown. Recent work indicates that large unbalanced doses of one or more of the components of vitamin B complex may be injurious to the liver.⁵⁵ During the acute stage of the disease a reasonable therapeutic formula, modified after Jolliffe,⁵⁶ seems to be the administration of 30 mg. of thiamine chloride, 10 mg. of riboflavin and 100 mg. of niacin, 300 mg. of vitamin C, 50,000 units of vitamin A and 2000 units of vitamin D.

To date the results of therapy with choline chloride and methionine in acute infective hepatitis have been equivocal,^{56, 57} and until more data are available methionine contained in high-protein diets seems to be an adequate and practical source of this expensive amino acid.⁵¹

SUMMARY

Under the term "infective hepatitis," two acute types are discussed: epidemic (and sporadic) hepatitis, transmitted in all probability by the intestinal-oral route, and serum hepatitis, transferred parenterally. Although these forms of hepatitis are alike pathologically and clinically, certain differences are summarized, since the infective agent has not been actually isolated, it is not clear whether the disorders are caused by the same or different etiologic agents.

The clinical and laboratory features of acute infective hepatitis are discussed, and it is pointed out that, contrary to military experience, cases encountered in civilian life may present serious diagnostic problems.

Prevention of infective hepatitis presents many difficulties, but certain preventive measures are of importance, especially in the parenteral transfer of serum hepatitis.

There is no specific therapy for infective hepatitis, but a program of adequate bed rest and proper diet is effective in the management of the disease.

Acute infective hepatitis is becoming more prevalent in civilian practice. It carries with it a serious morbidity and is probably an antecedent factor in chronic liver damage and cirrhosis more frequently than it is realized. The disease is treacherous and, at times, fatal, especially in old and debilitated patients.

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valuable aid in diagnosis and in the evaluation of liver damage

In the preicteric stage and in cases of infective hepatitis without jaundice, the laboratory can be of special assistance. The demonstration of bilirubin⁴⁰ and abnormal amounts of urobilinogen in the urine,³⁷⁻³⁹ positive cephalin-flocculation⁴⁰ and thymol-turbidity⁴¹ tests and the abnormal retention of bromsulfalein (as modified by Barker²²) are the most significant laboratory findings.

In the icteric stage of infective hepatitis the degree and course of jaundice can be followed most accurately by serum bilirubin determinations.⁴² The cephalin-flocculation and thymol-turbidity tests are positive with few exceptions in acute hepatitis but are usually negative in extrahepatic obstructive jaundice unless it is of long standing or associated with ascending disease of the biliary tract. The serial determination of urinary and fecal urobilinogen is one of the most useful laboratory aids in the detection of liver damage and in determining the character of obstruction.³⁸

A number of routine laboratory procedures and other liver-function studies may be utilized in special problems. Sometimes, as Watson⁴³ aptly states, "One might say that it was necessary to take a vote of the various functions of the liver in order to determine its ability to work as a unit." In any event, the proper use and interpretation of laboratory tests in relation to a careful history and physical examination ensures a correct diagnosis in the vast majority of cases.

PREVENTION

Since the infective agent has been demonstrated in the stools of patients with epidemic hepatitis during the preicteric and early icteric phases and possibly in nasopharyngeal secretions and urine, patients should be isolated, and dish, bedpan and urinal precautions employed at least during the acute stage. Water-borne epidemics due to contamination of the water supply have been described in camps, and since ordinary methods of purification of water do not destroy the infective agent, precautions regarding proper camp sanitation should be strictly enforced.⁴⁴

In this era of parenteral therapy, the increasing prevalence of serum hepatitis, which is by all accounts the most pernicious form of the disease, is a serious problem in civilian practice. It is now well recognized that the disease is transmitted by whole blood, plasma and serum, regardless of the manner of preservation. Janeway⁵ and others⁴⁵ have pointed out that greater opportunity for transfer of the infective agent is offered by large pools of plasma obtained from a number of donors than by blood or plasma from a single donor. The difficulty in eliminating potentially infective blood donors is obvious, since the infective agent is present in the blood long before clinical or labora-

tory evidence presents itself.^{5, 12} Nevertheless prospective donors showing any of the clinical laboratory findings of infective hepatitis, as well as those who within a year have had jaundice have been exposed to other jaundiced persons who have themselves had blood, plasma or parenteral therapy, should not be accepted.

British investigators recently demonstrated that serum hepatitis can be transmitted by contaminated syringes.^{46, 47} This imposes the obvious duty on office, clinic and hospital practice of using only properly sterilized syringes for intramuscular, subcutaneous and intravenous work.

The value of gamma globulin in the prevention of epidemic hepatitis has been well established,^{5, 48} and in civilian practice under epidemic conditions gamma globulin could be used. Recent reports indicate, however, that gamma globulin is not protective against serum hepatitis.¹⁹

Oliphant⁵⁰ has stated that ultraviolet radiation destroys the infective agent of serum hepatitis, and Grossman and Saward⁴⁶ suggest that this method be utilized to practical advantage. If feasible, this form of radiation may solve an extremely vexatious problem.

TREATMENT

There is no specific therapy for infective hepatitis but extensive clinical experience during the war has demonstrated the efficacy of intelligent medical care.

It is universally recognized that adequate bed rest is essential. No hard and fast rules are possible, but on the average three to six weeks are required before the active phase of the disease is over. When jaundice has cleared and the liver enlargement and tenderness have subsided, limited activity may be allowed and gradually increased over a period of seven to ten days. As Barker and co-workers^{22, 26} have clearly demonstrated, the real test of recovery from liver damage is tolerance for activity. During convalescence, if there is a return of any signs of activity of hepatitis, manifested especially by tenderness or enlargement of the liver, further bed rest should be required.

Liver-function tests may be employed to good advantage during convalescence. Clearing of bile and abnormal amounts of urobilinogen from the urine, absence of direct reacting serum bilirubin and normal excretion of bromsulfalein furnish the best laboratory evidence of recovery from acute infective hepatitis.²²

In the present state of knowledge it is difficult to evaluate the specific role of various dietary factors in the treatment of acute infective hepatitis. There is general agreement on the beneficial effect on the liver of large amounts of carbohydrate, and the value of a high-protein intake, especially one containing the essential amino acid, methionine, seems well established.^{51, 52} Fats, specifically those

population of diverse dietary habits and with great sectional differences in the types and amounts of foods available. In this country, moreover, we experienced an almost complete immunity to the hazards of war and the experiences of any noticeable hardships due to it, which certainly affected the attitude of our population toward its inconveniences. England's food-rationing program may have been stricter, but ours was undoubtedly more difficult to administer.

The Subcommittee on Medical Food Requirements recognized eleven conditions or groups of conditions that might reasonably require extra rations, and prescribed the upper limits of rationed foods that might reasonably be granted under the conditions existing in 1943. This list consisted of diabetes mellitus, active tuberculosis, chronic nephritis of the nephrotic type, cirrhosis of the liver, severe hepatitis, chronic ulcerative colitis, chronic suppurative diseases, sprue, obstructive gastrointestinal lesions, high intestinal fistulas and severe burns. No medical reason for any extra allotments of sugar was recognized, and it was even recommended that diabetic patients asking for additional rations forfeit their sugar allowance.

Another point emphasized by the committee — and this deserves special attention — was that its recommendations were intended only as a guide and should not be allowed to "vitiolate the scientifically necessary flexibility inherent in any wise system of rationing for the sick." The desirability of medical-appeal committees was also noted.

It is obviously impossible to determine how much rationed food any person may require without knowing first how much and what types of unrationed foods are available. When it is realized that the availability of unrationed foods varied from time to time and from place to place, that certain types of foods went on and off the ration lists, that point values were subject to frequent change and that human beings vary in their needs and capacities in disease as well as in health, it is understood how inaccurate rationing is at best, and how great is the need of flexibility in the system.

Stare,² nevertheless, in a lecture in 1943, showed how easily the average diet could be balanced, based on the traditional 70 gm. of protein a day and on a weekly meat ration of 840 gm., or approximately 1¾ pounds.

The committee of the Massachusetts Medical Society appointed to aid the district rationing officer was one of the first in the field, and from the beginning of its duties until now, when, it is fondly hoped, the duties are nearing their end, it has enjoyed the utmost co-operation from the Regional Office of Price Administration.

With little available precedent to follow when it first assumed its duties, the committee sought advice from various authorities in different branches of medical practice. The standards established for

diabetic patients, by far the most numerous group requesting extra allotments, were accepted as standards for most groups, and seemed to be in general satisfactory. These consisted of 32 pounds of rationed processed foods and 40 pounds of rationed meats and fats in total, including the normal basic allotment, for a two-month period. This allowance, which at that time practically doubled the basic rations, was found to be consistent with the allowances suggested by the Subcommittee on Medical Food Requirements when these recommendations made their appearance.

Local rationing boards were given the privilege of granting up to these maximum amounts on certificates of necessity properly filled out by registered physicians, and all other requests were regarded as those that should properly be reviewed by the medical committee. Since the number of certificates thus honored rose to an alarming degree, however, the Office of Price Administration limited to diabetes and active tuberculosis the conditions for which boards could grant requests, within the quantitative limits established by the medical committee.

A *cause célèbre* was furnished late in 1943 by the application of a defense plant for extra meat allowances for several hundred of its employees. The certificates presented for each of these men, who worked long hours at the open forge and in the heat treatment of metal, was for 3 pounds of rationed meat a day, on the basis of undue fatigue and extreme loss of weight. At that time the basic *weekly* ration was approximately 1½ pounds of meat, fats and oils. It is, of course, absurd to maintain that a diet adequate for a stenographer should also be adequate for a steel worker. Such a policy may be democratic, but it is not equitable. It seemed to the medical committee, however, equally absurd that the steel worker should require over fourteen times as much rationed meat as his fellow patriots.

This problem was studied by the Harvard Fatigue Laboratory, the State Department of Labor and Industry and the War Food Administration, which found that no supplemental ration need be supplied because of a consumer's occupation. Subsequently, the Office of Price Administration made provision for workers in industry by permitting employers to set up in-plant feeding operations where more generous per-capita allowances were made than obtained in commercial restaurants.

The scope of the advisory committee's functions increased, perhaps because of its own lack of sophistication in failing to escape added responsibility. Having been appointed in May to aid the district rationing officer, it found in October that the district had been enlarged to include all the Commonwealth, shortly thereafter, the district office was merged with the regional office, and a committee appointed by the president of the Massachusetts Medical Society soon found itself, vicariously, also

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SOME OBSERVATIONS ON THE RECENT FOOD-RATIONING PROGRAM*

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ON March 1, 1943, this country entered a revolutionary period in its history, for on that day it embarked on a food-rationing program that was to last two and three-quarter years, and on which the final word has not yet been spoken. Then, as the *Journal of the American Medical Association* phrased it, "the public's traditional peacetime latitude of dietary choice, limited only by ability to pay, was abruptly curtailed," and the Office of Price Administration became the official agency to administer the new program of point rationing.

Sugar, a luxury article of diet, had already been rationed for nearly a year, at the present time, nine months after V-J Day, sugar is the only rationed food, although the balance between supply and demand of other foods is still far from satisfactory, even in this food-producing country, and countless millions of the world's inhabitants face the worst famine in history.

Almost immediately, when rationing went into effect, the problem was encountered of consumers who were unable, or who considered themselves unable, to subsist on the allotted rations and claimed special consideration because of "medical necessity." Extra allowances for those who required them on the grounds of sickness were accordingly granted on a physician's certification of necessity, but the subsequent avalanche of requests showed the need for some method of controlling this dietetic enthusiasm. It became apparent that medical panels would be needed to sift the applications, to advise

the administrative authorities on the apparent justice of the various claims and to aid the medical profession in its own task of selecting patients and physical conditions that might require a tempering of the rules necessitated by the national emergency.

Logically, the state director of the Office of Price Administration sought the help of the president of the Massachusetts Medical Society, who appointed a committee to aid the district rationing officer in May, 1943. On the national level the Office of Price Administration called on the National Research Council for assistance, and the Subcommittee on Medical Food Requirements was appointed within the Division of Medical Sciences. This committee was organized in April, 1943. Its recommendations were published in the *Journal of the American Medical Association*¹ in October and were accepted by the Office of Price Administration on March 30, 1944, thirteen months after the advent of the rationing program. However fine the mills of the gods may grind, they certainly grind exceedingly slow.

The subcommittee was fortunate in having had the precedent of the Special Diets Advisory Committee of the British Medical Research Council to guide it to some degree. The British program worked well, but certain fundamental differences existed between the British situation and our own. Great Britain depends largely on the importation of food, and during the war the Ministry of Food owned some 98 per cent of the imported supply. Furthermore, Great Britain is geographically small and thickly settled, with relatively uniform dietary habits. The United States, on the other hand, is primarily a food-producing country with a mixed

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hoarseness (The opportunity for a pun is obvious, but a pun is still considered the lowest form of humor.) Other requests included 1 pound of processed foods and 31 of meats and fats a week for a patient with hemiplegia, 40 pounds of processed foods and 12 of meats and fats for another with hypertension, 31 pounds of processed foods and none of meats and fats for a pyelonephritic patient with renal calculi, 9 pounds of processed foods and no extra meats and fats for a patient with duodenal ulcer, and 12½ pounds of meats and fats and none of processed foods for another with the same disease. Too often, no rhyme or reason could be discovered for the types or quantities of foods solicited.

This particular committee of the Society believed that its functions were to advise and not to police, to make exceptions to any specific policy when a reasonable doubt seemed to exist in any given case and to err on the side of possible indulgence to prevent injustice, and yet to protect the interests of the majority. Our experiences also led us to believe that actually few persons could not have subsisted comfortably on their basic allotments, procured with reasonable intelligence, regardless of the disease.

Our observations further taught us that a danger is inherent in bureaucratic institutions, a propensity that must be curbed to regiment one's fellows and to derive satisfaction and a sense of duty done from the exercise of authority.

* * *

Certain conclusions based on our food-rationing experiences seem warranted. It is apparent that many, perhaps the majority of physicians are not well grounded in dietetics, particularly regarding the role and the quantitative application of the diet in disease. This fault is presumably one of basic medical training. At the same time, we must face the probability that wide gaps still exist in the available knowledge of the role that diet plays in disease. It is conceivable that some of the ideas that tradi-

tion has fixed strongly on us may at some future time be discredited. We must moreover accept the possibility that pressure that is hard to resist is not infrequently put on the physician to induce him to sign statements that may not entirely accord with his better judgment.

Many persons who are faced with the responsibility of marketing have little knowledge of this domestic function, of food values or of the planning of diets. Much more assistance should be made available to the public, nutrition centers should be one of the important municipal enterprises.

The value of fortified oleomargarine as an acceptable table fat has been demonstrated, and it should be allowed by law to compete on more nearly equal terms with other fats used for the same purposes. During the rationing period this committee accepted the point value of margarine as its standard for table fats.

There is justification for believing that occupational and perhaps other qualifications should be allowed to affect strict rationing principles. In the face of total war, the policy of lavish provision for military personnel at the expense of the civil population deserves reconsideration.

The war and subsequent events have brought to the fore some of the problems that had previously existed concerning the dangerously large and growing world populations and their source of food. The consumption of an abundant food supply by favored groups and nations while others starve may never again be permitted, some degree of food rationing will be perpetually necessary if Nature's stern laws are to be held in abeyance, and if succor is to be given those who else would fain have filled their bellies with the husks that the swine did eat.

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advising on the rationing difficulties of the four New England states that had failed to provide themselves with committees of their own. In August, 1944, it became, in addition, part of a larger committee organized to aid the War Food Administration in controlling the cream situation.

In the meantime, however, local committees were being appointed in strategic localities, largely through the good offices of the War Participation Committee of the Society, until eventually Brockton, Brookline, Haverhill, Lawrence, Lowell, New Bedford, Newburyport, Pittsfield, Springfield and Worcester were thus more or less autonomously served. As time went on, Maine, New Hampshire and Connecticut also established medical panels along a similar pattern. The Rhode Island office had been working successfully with the state medical society since the early days of rationing.

The population of Massachusetts at the time of the 1940 census was 4,374,000. Of this population, 13,500 persons were known to be receiving supplemental rations in September, 1944, and 18,898 in September, 1945, or less than 0.5 per cent. The rate of distribution of these extra rations showed the highest population percentage thus favored to come from cities of 15,000 to 25,000 population, with 0.5 per cent of the inhabitants in the privileged class, and the lowest receiving second helpings to come from cities of 5000 to 10,000, with only 0.2 per cent. Most of the acute rationing problems seem also to have come from the cities with 15,000 to 25,000 population. The Regional Office, from May, 1943, through August, 1945, processed 16,290 applications, of which about half were individually reviewed by the committee and the rest according to suggestions emanating from the committee.

It is also a matter of interest to learn that, after the virtual end of rationing, when the affairs of most of the local boards had been wound up, over 2000 unsuspected beneficiaries of extra sugar allotments turned up at the regional office for renewal of their unauthorized certificates.

Various factors in the food-rationing program created confusion and added to the difficulties of its administration. For those not infrequent persons who are ordinarily unable to clear the hurdle of counting their change after a purchase, the use of two forms of currency, points and pence, to be applied to pounds and ounces was almost more than could be endured. The frequent shifting of point values as different types of food became more or less available affected the extra allowances that were necessary to balance the various diets of "medical necessity." The inclusion of meats and fats on the same ration lists may have simplified the book-keeping of the program, but it made no sense when the balancing of a diet was contemplated. Life may simply have been rendered more piquant to the average housewife when she was made to choose between beefsteak and butter, but the two forms of

food had quite different meaning for the diabetic patient.

The one distinguishing feature of all processed foods was that they had to be preserved in some way, from canning to drying, and with fresh fruits and vegetables usually available, it soon became apparent that their value and desirability was rather an economic than a medical one. Actual justice based on individual merits was scarcely more evident in rationing than under a free economic system alone. The infant from the moment of birth, as a potentially free citizen of a country determined to be free, was given the same number of ration points as a manual laborer or a seasoned politician. The family of twelve had infinitely more variety in its point purchasing power than the spinster alone in her one-room apartment. The poorest farmer could live better than the richest banker, if the latter refused to patronize the black market.

Various abnormal physical conditions recurred as bases for extra-diet requests, and this committee believed that it was justified in departing, not infrequently, from the path marked out by the Subcommittee on Medical Food Requirements. Consideration was given to severe anemias of any type, to ulcer either recently postoperative or with recent hemorrhage, to allergy if specific clinical manifestations substantiated the request, to pregnancy in the latter half of the period of gestation, to rheumatoid arthritis with hypoproteinemia, weight loss or anemia, to malaria only on the basis of severe anemia and to demonstrated hypoproteinemia. Hypoglycemia, on the basis of recent advices, was usually considered to justify extra protein rations, rather than extra sugar. Nephrolithiasis came to be used as a basis for extra protein to produce an acid-ash diet, and the Schemm high-protein diet was recognized as of value in the treatment of heart disease with congestive failure. Whenever a question of policy arose, it was the custom of the committee to consult with recognized authorities. It was frequently necessary to return applications for more specific information than had been given—for example, with the patient who was stated to be allergic to all unrationed foods.

Extra evaporated milk, on the red-point list with meats and fats, was frequently requested for infants but was rarely granted, since the basic allotment of points covered the recognized milk requirements for normal babies.

Rations were requested at one time or another for practically all known diseases and in all imaginable quantities. The program, indeed, furnished the ideal example of the universality of headache as a symptom of all diseases—only it was the committee that had the headache. Such requests were made as the following: 14 pounds of meat a week for a child for normal growth, 7 pounds for the treatment of frequent colds, 4 pounds for the treatment of heartburn, and 2 pounds for the treatment of

from various prisons have also repeatedly shown a high prevalence of tuberculosis among such groups. The confinement and frequent overcrowding of these institutions offer an excellent opportunity for spread of the disease, and since many prisoners are later discharged to their homes and community, the dangers are obviously great.

Despite an unprecedented high average income, there are still many people in the low-income group, and it appears that the Negro remains at the bottom of the scale. The result is that among Negroes of twenty to thirty-five years of age, 1 in every 3 deaths is due to tuberculosis. Surveys have also shown that there is a high prevalence of tuberculosis among the Chinese and Polish groups. Poverty and tuberculosis go hand in hand, and a family fairly well off before tuberculosis strikes is often reduced to dependency when the wage earner enters the sanatorium.

It is an accepted fact that decent housing, an adequate diet and just wages for acceptable standards of living are necessary to keep down the tuberculosis rate. There is no doubt that a potent factor in the remarkable reduction in the tuberculosis mortality in this country over the past fifty years is the improved living conditions that have prevailed. If the disease is to be further eradicated, greater effort will have to be made to abolish slum areas and crowded tenement districts. A geographic survey of Boston undertaken by the Health Department showed that the highest incidence of tuberculosis is found in the crowded districts of the South End, West End, Roxbury and South Boston.

Industry must play its part if a reduction in the morbidity and mortality of tuberculosis is to be realized. A pre-employment examination, including an x-ray film of the chest, should be required. Well established standards for ventilation, sanitation, health education, personal hygiene and fair wages should be enforced.

The tremendous economic and financial burden on the taxpayer when long hospitalization is involved is not fully realized by the general public. According to the National Tuberculosis Association, the economic loss to the family and community, in addition to the cost of treatment, amounts to \$10,000 for each death from tuberculosis. The number of deaths in the community multiplied by this figure will give the financial loss from tuberculosis during any year. Case finding is a sound investment on the part of any community. The earlier the case is diagnosed, the shorter the period of hospitalization. In addition, the number of cases will be definitely reduced, for the early segregation of the patient prevents spread of the disease to the family and the community.

The opportunity of practicing physicians to find cases of tuberculosis is unquestionably greater than that of any agency, in view of the many patients

that pass through their hands. It is regrettable that, time and again, patients are admitted to sanatoriums with far advanced tuberculosis after having been under treatment for months for chronic bronchitis. It is a safe policy for the physician to insist on an x-ray film of the chest in every case in which a patient's cough persists for more than two weeks. There are some physicians who, despite a cough lasting for months, will not order an x-ray examination until abnormal sounds are heard in the chest. Any physician who waits to make a diagnosis of tuberculosis by auscultation imposes a grave responsibility on himself—9 out of every 10 cases by that time are in the advanced stage. It is no credit to a physician when a patient or the family suggests, and even sometimes demands, an x-ray film of the chest after numerous cough mixtures have failed and then to find, to his surprise, existing tuberculosis.

Again, the physician will find it advantageous to insist on an x-ray examination of the chest every six months on all diabetic patients. The high incidence and rapid spread of tuberculosis in diabetic patients are well known. It is further recommended that a chest x-ray film be taken in all cases of pneumonia approximately three months after the patient has fully recovered from the illness, since it has been shown on numerous occasions that an attack of pneumonia has been the responsible agent in lighting up an old inactive tuberculous lesion.

Any board of health has a responsibility for those unable to obtain the services of a physician and also a responsibility to the physician to provide diagnostic facilities. Boston is fortunate in having an efficient and well managed health department that provides examination of the sputum, tuberculin testing, x-ray study and consultation services. This service is free, and the physician should make every possible use of it. The inability of the general practitioner to recognize the disease in the early stage seriously retards the eradication of tuberculosis.

The physician should be educated to the necessity of reporting all cases of tuberculosis to his board of health as soon as the diagnosis is established and should not wait to do so on the death certificate. Early notification is of the greatest importance in any control program. During the past year there were 411 fatal cases of pulmonary tuberculosis in Boston. Of this number 96, or 20 per cent, were reported after death. It does not take much imagination to see that no program will progress if 20 per cent of the cases of tuberculosis are reported after death.

Those engaged in tuberculosis work have long realized the deficiencies in the training of family physicians in the diagnosis and treatment of tuberculosis. A regularly scheduled course of lectures should be made available to all practicing physicians in the community. Such schedules can best be arranged

TUBERCULOSIS CASE FINDING*

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THE continuous decline in the mortality and morbidity from tuberculosis since the beginning of the century has been most gratifying. Comparison of present rates with those of preceding years has engaged the attention of all public-health and allied workers.

Less publicized and perhaps less understood generally are the facilities now available for case finding as compared with those of twenty-five years ago. At that time no well organized plan or agencies for intensified case finding existed. The major question was not where or how to look for additional cases but what to do with the known cases. The hospital beds were far from adequate. The case-finding work that was done in some of the larger communities consisted for the most part in physical examination of the chest and laboratory examination of the sputum. Few, if any, clinics were provided with or had access to x-ray equipment, and the equipment itself had not reached the stage of development that made x-ray study of the chest in appreciable numbers of cases practicable. Even when x-ray service was available, it was always employed to substantiate a diagnosis already confirmed by physical or laboratory examination. As the knowledge for the care of tuberculosis increased and improvement of x-ray equipment developed, interest in case finding among contacts of known cases began to be manifest.

For a period of several years the tuberculin testing and x-ray examination of thousands of children and high-school students was perhaps the most vigorously promoted phase of the program of tuberculosis control. The splendid attention children received as a result of this activity yielded valuable information and focused the investigation on what is known as primary tuberculosis. These studies showed the remarkable ability of the majority of children to bring primary tuberculosis under satisfactory control.

Increasing interest in the control of tuberculosis in college students is due in large part to the co-operative efforts of the Tuberculosis Committee of the American Student Health Association and college authorities. The number of colleges and universities with case-finding programs has increased from six to over three hundred in the past fifteen years. As a result of such routine programs in colleges, between 700 and 900 new cases of tubercu-

losis have been diagnosed annually during the past several years.

The aim of any well managed and effective control program is early case finding by mass x-ray examination, which has been of tremendous value in the study of thousands of workers in industrial plants and business offices. A splendid example of how industry and labor can co-operate in early tuberculosis case finding was the recent mass x-ray examination of 100,000 fur workers and their families in New York City. The survey was the culmination of months of intensive educational work. The unions mailed posters to all the shops, distributed handbills among workers and included information in every meeting notice. If this record can be accomplished in one industry in a community it can certainly be duplicated in others.

The release of information on tuberculosis by Selective Service boards after mass x-ray study of all inductees showed what can be accomplished in discovering early tuberculosis. The survey pointed out that 90 per cent of the men rejected for tuberculosis had minimal disease, whereas almost 90 per cent of the patients admitted to most of the sanatoriums in this country have advanced disease.

The recent appreciation of the fact that adults, rather than children, are chiefly responsible for the spread of tuberculosis is why control programs are focused on older age groups. Public-health laws should insist on the mass x-ray examination of all schoolteachers, food handlers and domestics—a surprising number of food handlers, such as cooks and waiters, are admitted to sanatoriums. Tuberculosis is found more frequently in certain occupations than in others. The danger of silicosis and tuberculosis is well known and much has been done to control the hazard of silica dust.

Student nurses and physicians are often exposed to massive infection in their daily duties. This problem has only recently been recognized in its relation to the general hospital or to the institution for the mentally ill. Every patient admitted to a general hospital should have an x-ray examination of the chest. In this manner, many new cases of tuberculosis could be discovered. If these cases could be detected on admission, it is quite reasonable to believe that the prevalence of tuberculosis among medical students and nurses would be greatly reduced.

X-ray films of inmates of mental hospitals should be taken from time to time, for recent reports have shown a high incidence of tuberculosis, these patients are a source of extreme danger not only for other inmates but also for the attendants. Surveys

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an appropriate loss in weight. Apparently, in many cases, such loss of weight is masked for as long as nine or ten days by a compensatory gain in body water, which is eventually lost, revealing the true body weight. There is also little evidence for the popular view that obese persons have a more efficient digestive mechanism that enables them to extract from their food a higher percentage of nutrient material.

It has also been suggested that adiposity is caused by a hereditary trait of the adipose cells by which they are enabled to accumulate excessive amounts of fat and retain it despite starvation. This suggestion has been disposed of by Newburgh.⁶ Obese persons were shown to be able to release fat into the blood when placed on a starvation diet, and the fasting respiratory quotients in fat persons were found to be lower than those in normal controls, indicating that fat was being used for energy purposes. According to Conn,⁷ abnormalities of the endocrine system, which affect adipose tissues, are more closely related to distribution than to excessive accumulation of body fat. The search for metabolic aberrations that could lead to obesity has therefore not been fruitful. The accumulation of fat appears in most cases to be the result of an overall intake of energy that has exceeded the total dissipation of energy by the body, with the result that the excess energy has been stored in the form of fat. The fundamental fault therefore seems to be largely an excessive desire for food. This factor is suggested also by the careful study of Danowski and Winkler⁸ on the long-term management of obese patients. Neither the central nervous system nor endocrine factors were significantly involved in the 141 patients included in their study, and in most cases it was found possible to effect weight reduction by restriction of the caloric intake. In almost all cases, however, there was a failure to maintain weight reduction, and the authors emphasized the difficulty of effecting significant changes in the dietary habits of their patients.

A number of recent studies throw light on the important question of overeating or, for that matter, undereating. Basically, eating is instinctive, and it is not surprising, therefore, that there are strains of mice in which overeating and adiposity are hereditary and appear to be associated with a single gene that is identical with the one responsible for yellow color in mice.⁹⁻¹⁰ Severe and prolonged insulin hypoglycemia in mice leads to overeating and obesity,⁷ and hypoglycemia in man^{11, 12} also results in excessive eating and gain in weight. In 5 of the 6 cases presented by Rennie and Howard¹¹ a gain in weight was a striking phenomenon — the result of frequent eating to relieve the hypoglycemia.

One of the most fruitful approaches to the problem of obesity is the study of its association with the hypothalamus. The earlier experimental workers in this field were more impressed with the role of

the hypophysis, and a measure of evidence still implicates this organ. Thus, in the experiments of Heinbecker, White and Rolf¹³ on experimental obesity in the dog, it was found that either removal of the hypophysis or production of a lesion of the hypothalamus, resulting in partial or complete destruction or denervation of the paraventricular nuclei of the hypothalamus, caused obesity. The additional bilateral destruction of the supraoptic nuclei enhanced the rate of development of the obesity. The maximum degree of obesity followed a properly placed hypothalamic lesion without removal of the hypophysis, but following such a lesion a diminution and degeneration of the basophil cells of the hypophysis occurred. The enhanced rate of development of obesity occurring with damage to the supraopticohypophyseal system is of interest inasmuch as this nervous pathway is responsible for the control of the antidiuretic-hormone-forming tissue of the hypophysis and because diabetes insipidus resulted when it was cut. Obesity may, however, be produced without the participation of the hypophysis, as shown by the experiments of Hetherington and Ranson,¹⁴ who placed lesions in the ventromedial hypothalamic nuclei and later hypophysectomized the animals. After the usual interval of three to six weeks following the hypothalamic operation, all the hypophysectomized animals became progressively fatter until a high degree of adiposity was attained. In subsequent experiments reported by Hetherington,^{15, 16} hypothalamic obesity was produced in rats already displaying chronic hypopituitarism as the result of hypophysectomy. During a period of approximately eleven weeks after removal of the hypophysis, no signs of obesity appeared, but shortly after hypothalamic lesions were made, obesity began to appear.

Brobeck and his co-workers¹⁷ have shown that the essential cause of the gain in weight of hypothalamic animals is an increased food intake, although there may be an associated reduction in activity. When hypothalamic rats are pair-fed, that is, given only the amount of food taken by a normal rat, they do not gain in weight, but become obese only when they are given access to an unlimited supply of food. The characteristic change in the food habits of these animals was that they voraciously attacked their food and ate large quantities in a short time, comparable to the episodes of bulimia observed by Brügger¹⁸ produced by electric stimulation of the hypothalamus. Wheatley¹⁹ noted that cats with hypothalamic lesions became fat, as did monkeys studied by Ruch, Schenken and Patton.²⁰

By analogy with the sham rage of decorticate and hypothalamic cats noted by Bard²¹ and other workers, it might be postulated that excessive eating in this condition represents the release of lower mechanisms from control by hypothalamic nuclei and that, in turn, these centers are released from inhibitory influences from higher levels of the brain.

through the district medical society. It is safe to say that a good number of general practitioners do not even know what the inside of a sanatorium looks like. The physician should certainly avail himself of the opportunity to visit the nearest sanatorium from time to time and see for himself what is being done for the patient with tuberculosis.

Medical schools should avail themselves of the best and most effective method of teaching the essentials of diagnosis and treatment of tuberculosis. It is unfortunate that the great majority of graduates of medical schools do not have a sufficient understanding of tuberculosis. This situation seems to be due to the fact that the medical graduate is often told that tuberculosis is a waning disease that will completely disappear in a few years, medical students twenty-five years ago heard the same story. There is no doubt that tuberculosis is still the most serious health problem confronting any state or community. One cannot overlook the fact that there are still about 500,000 cases in the United States, that tuberculosis is the leading cause of death between the ages of twenty and forty

and that on the average nearly 60,000 persons die of tuberculosis every year.

The public must be constantly and increasingly educated in the danger and contagiousness of tuberculosis. When the disease strikes a member of a family, interest is aroused, but even then the members frequently fail to heed the danger that threatens them. The motion-picture industry could and should play an important role in the production of films available not only for teaching purposes but also for impressing on the public the value of tuberculosis case finding.

* * *

It is obvious that the crux of any program of tuberculosis control is early case finding by mass x-ray study and immediate segregation of the patient until he is well enough to return to his family and community. If a reduction in the mortality and morbidity from tuberculosis is to be achieved, the full support and co-operation of the general practitioner, the public, industry and public-health agencies are absolutely essential.

MEDICAL PROGRESS

PHYSIOLOGY*

HEBBEL E. HOFF, M.D.†

MONTREAL, CANADA

A CONSIDERATION of current publications that describe physiologic investigations carried out under the impetus of war suggests that, in this field as in others, greater progress was made in the application of known basic principles than in the discovery of new material. This is not, however, entirely the case. Thus, the pharmacologic screening of thousands of previously untested toxic compounds for potential value as chemical-warfare agents has uncovered many that hold promise as therapeutic agents or as tools in future physiologic investigations.¹ The great practical advance in the production of radioactive material will certainly be of inestimable value in the study of the biologic relations of these substances.²⁻⁴ Undoubtedly, the war has also hastened the recognition of the essential unity of psychologic and physiologic processes and the appreciation of the importance of psychosomatic relations in disease. Some of these are briefly reviewed.

OBESITY

The recent report by Levy, White, Stroud and Hullman⁵ on the increased incidence of cardio-

vascular disease associated with obesity in a study of 22,000 officers in the Army adds further evidence to the accumulating data pointing toward the unfavorable influence of obesity on length of life.⁶ It may of course be argued that obesity and cardiovascular disease represent two manifestations of a single etiologic factor operating through some genetic or psychosomatic mechanism and that control of the obesity has less than the expected influence on the cardiovascular system. The common-sense view of the matter, however, seems to be that since obesity requires an increase in metabolism to maintain itself and therefore demands an increased cardiac output, it is only reasonable to suppose that this constant additional strain proves harmful in the long run, especially when for some other reason the efficiency of the cardiovascular system is reduced. Metabolic studies in obese patients tend to discount the presence of any important alteration in metabolism in the great majority of cases.^{6,7} Obese patients in general do not show a lower energy expenditure than normal persons of the same height, age and sex, on the contrary, their total expenditures of energy are greater. If they are placed on a low-calorie diet and their weight determined over a long period, they do not fail to show

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Cutting²⁸ and Spiegel and Oberndorf³⁰ At the least, the evidence they present makes it impossible to accept the earlier conclusion of Daniels³⁹ that the manner in which such patients faced the problems presented by their infirmity indicated that they were of a stable nature. Apparently, other aberrations of the sleep mechanism may be involved in much the same manner. Thus, Ingram, Barris and Ranson⁴⁰ were able to produce catalepsy—a somnolent state characterized by loss of voluntary motion and sensibility and a peculiar plasticity of the skeletal muscles—by lesions of structures in the neighborhood of the mammillary bodies, such as the posterior hypothalamic nucleus, the supra-mammillary area, the lateral hypothalamic area and the region caudal to the mammillary body. A somewhat similar clinical condition called sleep paralysis in which, on awakening, consciousness returns some seconds before the return of voluntary motor power seems to occur in persons intensely disturbed by confusion in emotional direction.^{41, 42}

It is to be understood that the hypothalamus can be called a "center," so far as such functions as sleep and appetite are concerned, only in the sense that it serves as a final common path for such activity and not as the center in which activity originates, and that essentially similar results are obtained by lesions that interrupt pathways between the hypothalamus and receptor organs, by damage to the hypothalamus itself⁴³ and by lesions interrupting pathways between the cortex or other structures and the hypothalamus⁴⁴ or psychologic disturbances involving eventually the same pathways. Even when the basic lesion is anatomic, as in a case quoted by Aring and Engel,⁴⁵ psychotherapy has an important role to play, but on the other hand, medical therapy has an equally valuable role to fill when the etiology is of purely psychologic origin as illustrated by the success of amphetamine (Benzedrine) sulfate in the treatment of narcolepsy and obesity.⁴⁶

TREATMENT OF PEPTIC ULCER

The salient features of peptic ulcers might be outlined almost exactly as the preceding topics.⁴⁷⁻⁴⁹ In experimental animals and in man, gastrointestinal ulcers are sometimes produced by lesions of the hypothalamus. Cortical lesions also cause disturbances in the gastrointestinal tract, presumably by interruption of fibers passing to the hypothalamus. Such lesions upset a normal level in parasympathetic balance, leading to excessive secretion and motility and, perhaps, excessive vasoconstriction in the mucosa resulting in local anemia that renders the mucosa digestible by its own juice. A vicious circle is set up by the feeding back into the central nervous system of abnormal impulses from the gastrointestinal system arising either from pain or from hypermotility, which, in turn, intensify the nervous imbalance that was the primary cause of the ulceration. The situation thus becomes autonomous—

that is, capable of continuing after the precipitating factor has disappeared.⁵⁰⁻⁵² In man the same neural pattern may be involved in a neurotic reaction to produce and maintain gastrointestinal lesions. Medical treatment is of value as an adjunct of psychotherapy by helping to stop the vicious circle by interrupting it at some peripheral point. The psychoanalytic concept of the etiology of peptic ulcers is reviewed as follows by van der Heide.⁵³

Under the influence of certain unhappy experiences, interfering too much with a natural development, a child can be forced to fall back in its emotional maturation. This may sometimes increase such wishes as to be cared for, to be loved, to depend on others, to receive and—if thwarted—to take aggressively (regression to oral receptiveness and oral sadism). Whereas the ego reacts to such tendencies with feelings of inferiority and guilt, these are repressed from consciousness, sometimes under seal of a strong overcompensation, manifest as an independent, efficient, later responsible and giving attitude in life. This type of "conflict-solution" was regularly found in the gastric patients whose unconscious longing for care, love and dependence could not be concealed from the analytic observation. Next to the described internal reaction, sometimes external factors were found to be capable of maintaining a fatal frustration of those infantile cravings. The latter, obviously, once in life are perfectly gratified, namely, at the time of being nursed, when almost indistinguishably love and food are abundantly offered. Alexander states, "The wish to be loved becomes emotionally associated with the wish to be fed." If wishes for care and dependence are now strongly repressed, we may assume that these easily activate, or rather are "converted into" the desire to be nourished, which as a continuous unconscious psychic stimulus, influences the secretory, muscular and vascular condition of the stomach by means of the vegetative nervous system until it behaves "as if it were taking or were about to take food." Such chronic functional gastric disturbances, besides being likely to cause neurotic stomach complaints, appear to be of essential importance for the development of gastric and duodenal ulcers.

These factors are illustrated in the history of 2 cases reported by van der Heide in which the stomach complaints preceding the occurrence of an ulcer arose when the incongruity between the overt behavior (struggle and ambitious efforts for accomplishment) and the repressed longings for dependence became excessive.

In great measure because of Cushing's⁵⁴ concept of excessive vagotonia as the principal precipitating factor in the etiology of peptic ulcer, attention has recently been turned to the surgical section of the vagus nerve as the most effective means of arresting this hyperactivity.⁵⁵ A recent report by Thornton, Storer and Dragstedt⁵⁶ strongly suggests that the most important etiologic factor in the genesis of ulcer is the continued hypersecretion of acid during the night. They found that this hypersecretion is almost entirely neurogenic in character and is greatly reduced by section of the vagus nerve. The empty stomach of ulcer patients also displays a hypertonicity and hypermotility, with exaggerated hunger contractions, and these functions return toward normal after bilateral vagotomy.

On purely theoretical grounds atropine might be expected to be as effective as surgical section of the nerve, but this expectation is not fulfilled. This may

with the production of a similar condition Ferencz et al²² noted, in fact, that marked obesity developed in two decorticate cats kept alive for over a year

The only significant metabolic change noted in hypothalamic animals has been an abnormally large elevation of the respiratory quotient appearing after the administration of glucose,^{23, 24} but it appears that this alteration is secondary to the altered eating habits of the animals and that when normal animals are trained to eat in the same fashion they show a similar carbohydrate response

Most interesting is the observation that syndromes closely resembling those produced by anatomic lesions may appear as the result of psychologic stresses in the absence of an anatomic substrate. Thus, it is impossible to find frank hypoglycemia in all cases of so-called "hypoglycemic fatigue," although an altered sugar-tolerance curve like that of frank hypoglycemia may be seen. In a number of these patients the personality make-up was one of a conscientious, hard-working but dependent person in whom the difficulty was precipitated by increased responsibilities and withdrawal of protecting influence. Fatigue thus served to excuse the patient for nonperformance of tasks that had become distasteful, but it also served to make matters worse and thus set up a vicious circle of increasing fatigue and increasing distaste for work. At times, in such circumstances, medical treatment broke the vicious circle by reducing fatigue and was therefore an essential counterpart of psychotherapy

Psychologic factors may also be recognized in the precipitation or intensification of attacks in patients in whom some underlying disease exists, as in the cases reported by Meyer, Bollmeier and Alexander,²⁵ in which a definite correlation between the emotional status and the quantity of sugar appearing in the urine of diabetic patients could be made out, and in the case reported by Romano and Coon,²⁶ in which attacks of hypoglycemia were produced by emotion in a patient who was later found to have a pancreatic tumor. A much closer approximation to actual anatomic syndromes was observed in certain cases of narcolepsy, discussed below, in which the syndrome of abnormal sleep, obesity and polyuria may develop on a purely psychologic level.²⁷⁻³⁰ This also occurs in anorexia nervosa, which closely simulates Simmonds's disease.³¹⁻³³ It has been postulated that rejection of food is an expression of fear of pregnancy based on childish concepts of oral impregnation. It is interesting that in most of the cases of anorexia reported, periods of rapid weight gain, sometimes to the point of obesity, and of compulsive eating of large quantities of food have occurred along with excessive drinking of water. It is clear that appetite and eating represent a fundamental primary instinctive drive to which an early sexual association is attached. In

addition, eating is one of the first ways in which an infant is brought into association with other persons, and it develops, therefore, into an important medium for social expression. It is not to be wondered at that eating becomes much more than a process whereby the body is supplied with an adequate number of calories and vitamins

SLEEP

The sleep mechanism is another example of an essentially instinctive mechanism — heavily weighted with emotional and social values — that may become disturbed at anatomic, physiologic or psychologic levels. It is well established that on the anatomic level the hypothalamus is intimately associated with sleep and that increased somnolence can be caused by damage to the hypothalamus in regions that on stimulation produce hyperactivity.^{34, 35} It has also been observed that pathologic sleep may be associated with lesions in the cortex without invasion of the hypothalamus and in the absence of increased intracranial pressure.³⁶ Such observations led Davison and Demuth³⁶ to the conclusion that some fibers for the control of sleep originated in the cerebral cortex, especially in the hippocampal, cingular, premotor and temporal convolutions, and that injury to these areas or to their connections with the hypothalamus occasionally caused pathologic sleep. The psychologic value of sleep is manifest at a number of levels. Superficially it affords rest and recuperation, on a deeper plane, it furnishes a means of escaping from reality and represents a return to intrauterine life or even a type of death.³⁷ It thus affords a means of unconsciously satisfying forbidden wishes without experiencing conscious guilt. These concepts are clear even in the pre-Freudian psychology as can be seen by the following translation from Burdach's³⁸ treatise published over a hundred years ago

Periodicity ought thus to consist of an alteration of propulsion, which leads to development, and of retrogression, which leads backward toward the embryonic life. In fact, life tends to progress, but it also attempts to remain the same, and this latter tendency is the actual cause of all periodic retrogressions. Since the most general attribute of the organism is to conserve itself, — that is to say, to maintain itself by its own activity, — the primordial form of existence ought to be that which is always dominant, that which attempts to maintain itself throughout life. But this enters into conflict with the purpose of life, which can only be attained by progressive development, and the hindrance which it thus experiences permits it to manifest itself only with a periodic character. Periodicity is thus the expression of the conflict between development, expressed by exhaustion, and the return to the primordial state, which is manifested by contraction

Periodic return is therefore a suppression of antagonisms, an effacement of differences during which life reunites its forces for a new step along the road of development. Just as Geryon, son of the earth, felt the return of his strength when he touched the breast of his mother, so also the organism is rejuvenated in its return to the primordial state. The direction from within outward is a finite force that is dissipated by the very act of its own manifestation, and it renews its vigor only if the life withdraws into itself

The psychogenic nature of narcolepsy seems to be well established in the cases reported by Davison,³⁷

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Fourteen months before entry the patient had been operated on at another hospital for rupture of the intervertebral disk between the fourth and fifth lumbar vertebrae on the left. Following the operation she continued to have low-back pain on coughing or straining. The leg pains subsided but returned a few weeks later. Seven months later the pain had extended into the calves and was so severe that she remained in bed for two months, getting up only to go to the bathroom. Then she gradually undertook more activity, but the legs were weak and felt as if they were about to buckle. Five months before entry she began to have difficulty in controlling the bladder and subsequently was occasionally incontinent of urine. She also noticed numbness over both thighs from the iliac crests to about 15 cm above the knees. This and the incontinence subsided spontaneously after six weeks. The weakness of the legs progressed, however, and four months before entry the patient was able to walk only with a cane and the help of another person. She also had severe pain in the lower

lumbar region, sometimes radiating up to the costal margins and aggravated by straining but not coughing. Bladder and bowel functions were good except for constipation, which was controlled by laxatives.

Except for marked tenderness over the lower lumbar spine, the abnormal findings on physical examination were confined to the lower extremities, which were pale and cold. All motions of the feet, legs and thighs were extremely weak, there was no complete paralysis. Both knee jerks and the right-ankle jerk were absent, there was a weak left-ankle jerk. The plantar reflexes were absent. Sensation was impaired below the groins.

The temperature, pulse and respirations were normal. The blood pressure was 110 systolic, 80 diastolic.

Examination of the blood showed a white-cell count of 8400, with a hemoglobin of 12.4 gm. The serum nonprotein nitrogen was 27 mg per 100 cc. The urine was normal except for a + test for albumin.

On x-ray examination the pedicles of the second and third lumbar vertebrae on the right could not be clearly seen and appeared to be partly destroyed. In the lateral view there was a slight deformity—suggesting erosion—of the posterior border of the body of the second lumbar vertebra. A puncture at the third lumbar vertebra produced slightly hemorrhagic xanthochromic fluid, which clotted on standing. There was no rise in pressure on jugular compression. The total protein of the fluid was 5880 mg per 100 cc. Five tenths of a cubic centimeter of Pantopaque in oil was injected, and on lowering the head end of the table this was arrested opposite the upper margin of the third lumbar vertebra.

On the sixth hospital day an operation was performed.

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A PHYSICIAN Was the tumor in the filum terminale?

DR. MIXTER It seemed to be. It was difficult to be sure whether it arose from a small nerve root or the filum terminale. The nerve roots were plastered on the outside and had to be dissected off. It was equally distributed on the two sides, behind and in front. The tumor did not look like a neurofibroma.

CLINICAL DIAGNOSIS

Tumor of cauda equina

DR. SEMMES'S DIAGNOSIS

Ependymoma of filum terminale

ANATOMICAL DIAGNOSIS

Ependymoma of filum terminale

PATHOLOGICAL DISCUSSION

DR. KUBIK The tumor was 5 cm long and about 11.5 cm in diameter. Histologically it chiefly consisted of small follicles of cells with well stained cytoplasm, in some places there were elongated cells whose bases rested against the adventitial connective tissue of the blood vessels. Our diagnosis was ependymoma. The appearance was suggestive of a slowly growing, relatively benign tumor. Some of the cases of ependymoma of the cauda equina that have been followed for several years have not demonstrated clinical signs of recurrence.

CASE 32492

PRESENTATION OF CASE

A fifty-one-year-old housewife entered the hospital because of pain in the left lower quadrant of the abdomen and vaginal discharge.

Eight months before admission an acute attack of sharp pain in the left lower quadrant occurred. Thereafter the attacks were often repeated, sometimes before and sometimes after the menstrual period. The pain was always in the same area. Usually the patient wanted to lie down during the attacks, but occasionally sitting up gave relief. Each bout lasted nearly an hour or less. During the two months preceding admission, following a trip to Ohio, there was a mucosanguineous vaginal discharge, which came on gradually and was continuous.

There had been hot flashes for three years, and catamenia dwindling from a regular period of five to three days over five years. An appendectomy had been performed eighteen years before admission. Two children were living and well.

Physical examination was negative except for the pelvis. There was a mucopurulent vaginal discharge. The perineum was markedly lacerated. There were a cystocele and a urethrocele. The cervix was large, with many nabothian cysts. A rough granular area was seen on the right posterior cervical lip. An irregular, hard, firm mass that was felt in the region of the fundus was three times the size of a

normal fundus and seemed to project more to the left than to the right.

Routine blood examination was normal. The urine gave a + test for albumin, and the sediment contained numerous white cells on the first examination but three days later contained 10 white cells and 15 red cells per high-power field. The guaiac reaction of the stool was negative. A vaginal smear was reported positive for tumor cells, but a second smear contained too much blood for satisfactory examination. Biopsy of several areas on the cervix, including the granular area, was reported as showing chronic endocervicitis.

An operation was performed on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD ULFELDER This is the history of a fifty-one-year-old woman who was in the midst of the menopause, with hot flashes and some decrease in the length of the period, but still not missing a period, I gather. She had had two normal children. The only thing of interest in the past history is the fairly simple abdominal operation, which probably had nothing to do with the illness on admission. I take it that the patient had been well prior to eight months before admission, but that at that time she had an acute onset of pain in the left lower quadrant, which had recurred. I assume that there had been no associated gastrointestinal or urinary symptoms with these attacks. Their relation to the menstrual period must be considered, since they occurred both before and after the period. No mention is made whether they occurred during menstruation, however. In other words, they could have occurred at any time, so far as I can deduce from the record. They were well localized, always to the same area. They lasted for a variable period but never more than an hour, and there were no associated symptoms. Sometimes when lying down the patient felt more comfortable, but occasionally when sitting up she obtained relief. This means to me that it was not any one position that relieved the pain but rather a change of position that seemed to help. Although it is likely that the symptoms were associated with the pelvic mass, we must rule out extragenital sources for this picture.

Were intravenous pyelograms done? I wondered about that because of the few red cells and white cells in the sediment, and it is of interest, since these attacks of pain in the left lower quadrant could have been on the basis of genitourinary disease.

DR. TRACY B. MALLORY There was no pyelogram, and no barium enema.

DR. ULFELDER Assuming that we have more or less ruled out genitourinary causes of the symptoms, what could the diagnosis have been in a patient who had attacks of pain in the left lower quadrant, with some discharge that apparently was intermittently bloody, and who had a firm, hard pelvic mass, which felt like a fundus of three times the normal

suspicious of a tumor. Of course, this patient may have had some striking physical signs in favor of a ruptured disk, but in spite of this, with such a history, I think that this is a case in which a myelogram was indicated before operation. The record does not state whether a ruptured disk was found or removed.

It is significant that, following operation, the patient continued to have low-back pain on coughing and straining and that the leg pain was not relieved. That is not unheard of following removal of ruptured disks, but at the same time the patients usually obtain prompt relief.

Recovery from the paralysis of the bladder after a few weeks and improvement in the power of the legs are not incompatible with a tumor, since, paradoxically, periods of improvement are well known with tumors.

The constipation may have been the result of pain on straining, as in patients with cerebellar tumors, rather than paralysis of the colon.

It is to be remembered that this patient was explored on the left side for a ruptured disk in connection with the fact that the deep reflexes in the legs were lost, with the exception of the ankle jerk on the left.

Perhaps one should think of the possibility of a chronic osteomyelitis or an injury to the vessels, resulting in a false aneurysm or an arteriovenous fistula, since these accidents have been reported following operation for a ruptured lumbar disk. The later signs and symptoms, however, were at a higher level, and I think that they can be dismissed without further concern.

X-ray examination was reported to show erosion of the body of the second lumbar vertebra and the pedicles of the second and third. It would be helpful to know whether the bone destruction was caused by a malignant tumor involving the bone or by pressure atrophy such as that caused by large benign tumors in the central canal. On examining the x-ray films, it is evident that the bone changes were due to lateral pressure on the pedicles and forward pressure on the posterior surface of the second vertebra. The myelogram indicates an intradural, rather than extradural, tumor at the third lumbar level.

The spinal-puncture findings showed a complete fluid block, which was evidently of long standing, as indicated by the high total protein content. The presence of fresh blood in the spinal fluid suggests that the needle penetrated the lower end of the tumor or that there had been some sudden increase in pressure.

For a number of years, when encountering a fluid block, we have used injection of a few cubic centimeters of air (without a myelogram) and found that it is valuable in verifying the level by reproducing pain. In such cases the neurologic level is sufficient.

DR JAMES R. LINGLEY: These are the involved pedicles of the second and third lumbar vertebrae.

There is scoliosis, in spite of which there is evidence of thinning and erosion of the pedicles. In the lateral view the erosion on the posterior surface is not too well defined. In this film there is evidence of complete block at the upper level of the third vertebral body.

DR SEMMES: I believe that the patient had a long-standing tumor involving the cauda equina below and close to the conus, and that operation was certainly indicated. A variety of intradural tumors, including neurofibromas, ependymomas, meningiomas and gliomas, occur in this position. I was interested in knowing just where this one arose. The bilateral pain suggests that it was central, and the pain was certainly not like that from a neurofibroma involving an emerging nerve root, which would probably be attached to the filum terminale or one of the central filaments.

A PHYSICIAN: The neurologic level is much higher than the radiologic level. It seems to be somewhere around the upper part of the first lumbar vertebra. One might postulate that whatever the level was, a fairly long lesion was involved.

DR SEMMES: I am frequently content to know either the top or the bottom level of the tumor, preferably the latter, because it is easier to approach from below. It is unlikely that this was a round type of tumor, but one would expect a fairly long tumor—even longer than the neurologic changes suggested. I think that the pain at the costal margin was probably coincidental.

A PHYSICIAN: What would you say about the advisability of operating for herniated disk in a patient with bilateral pain and an atypical picture, without further investigation?

DR SEMMES: I tried to indicate that if a patient has a peculiar or atypical history, one should do a myelogram and consider the symptoms from various angles. In case of doubt, it is then a matter of exploration rather than operation for removal of a disk. I am not opposed to myelography, but I am opposed to unnecessary myelography.

DR CHARLES S. KUBIK: Dr. Mixter, do you wish to make any comments?

DR W. JASON MIXTER: It seemed to us when this case was presented at this hospital that it was a rather clear-cut case, as Dr. Semmes has suggested, of a tumor in the cauda equina, and that the previous operation might be criticized because it was done without a complete study. At operation the upper portion of the lumbar canal was exposed, presumably including the area of the twelfth thoracic vertebra, and a long slender tumor in the cauda equina, arising apparently from the filum terminale and doubling back on the conus, was exposed and removed.

DR KUBIK: What was the subsequent course?

DR MIXTER: The patient presumably made a fairly complete recovery. We were worried about the bladder, and I suppose that the reflex changes persisted.

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CLINTON'S NEW HOSPITAL

IT is with particular pleasure and satisfaction that we make mention of the ground-breaking ceremony, on October 16, for the new building of the Clinton Hospital. We congratulate Clinton on its new hospital-to-be, our special interest, however, lies in the fact that the ground was broken, physically and in person, by Dr. Walter Prentice Bowers, after whom this building will be named, who figuratively broke ground for the first Clinton Hospital, over

size? We cannot exclude cancer in a patient—not only of this age but also of any age—who has a bloody vaginal discharge, and I think that the diagnosis of either endocervical or uterine cancer must be entertained in this case. But if it was present I think that it was incidental rather than the basis for the symptoms, except perhaps for the discharge. I assume that this granular area on the cervical lip, where a biopsy had been reported as showing no evidence of cancer, explained the discharge. I cannot say that this woman did not have a cancer of the fundus or cervix, but if she did have cancer I do not believe that it explains all the symptoms. What then, in a woman of this age, is a mass, three times the size of a normal fundus, that is hard and firm? Statistically, it is a fibroid, which is more probable than ovarian tumor in this age group. On the other hand, even a pedunculated subserous fibroid would not cause the attacks of pain in the left lower quadrant of which this patient complained. I think that a solid tumor of the left ovary would be even harder and firmer than the one described. I therefore think that this is likelier to be a cystic tumor of the left ovary. The lack of endocrine effect—the patient had an uninterrupted progress of menopausal symptoms—suggests that this was not an endocrinologically functioning tumor and does not help in making the final diagnosis, it merely excludes a small group of possible pelvic tumors. My diagnoses are cystic tumor of the left ovary and possibly cancer of the endocervix or uterine fundus, which I cannot exclude or include on the basis of any information available. I shall not even discuss the smear.

DR. MARSHALL K. BARTLETT I should like to know how often positive vaginal smears are obtained in ovarian cancer.

DR. ULFELDER I cannot answer that because we have not correlated the ovarian lesion with smears, either positive or negative.

DR. BARTLETT We have seen some.

DR. ULFELDER Yes, but we have seen some either way. There is no relation suggesting that in the presence of ovarian tumor there is a distinguishable change in vaginal cytology. We have seen positive smears with ovarian cancer, but they were in cases in which the tumor had invaded the uterus, in direct continuity with the genital canal.

DR. CLAUDE E. WELCH How much significance does a positive smear have?

DR. ULFELDER Statistically, it is difficult to tell how significant it is. Certainly we can quote the findings and the figures in the presence of established cancer of either the cervix or the fundus. The smear fails to show evidence of cancer in 11.5 per cent. All I can say is that in our series, of a total of 2400 patients who did not have cancer that could be proved pathologically, 49 had positive smears. We went back over the 49 cases, and there were 30 that would not now be called positive

smears. They represent the error in learning a new method. But 19 of the patients had positive smears, which we were unable to confirm pathologically.

DR. MALLORY Speaking from the point of view of the pathologist, in cases in which we receive only a biopsy from either the cervix or the endometrium, there is always a possibility that the biopsy was not taken from the right place, and that may be one reason that we have failed to confirm some of the smear diagnoses. There have been a certain number of cases in which we have had the entire uterus to examine and in which, on routine examination, we have not found carcinoma. There is always, however, the possibility of a minute lesion, which could easily be missed in ordinary routine examination.

DR. WELCH I think that Dr. Ulfelder should be congratulated on his diagnosis. Examination under ether revealed the mass described in the record. The uterine canal was approximately 12 cm deep. Curettings were grossly normal. I assumed that we were dealing with multiple fibroids and that the mass in the left vault was a subserous leiomyoma. On opening the abdominal cavity it was obvious that there was a cystic tumor of the left ovary. On the uterus there were tiny fibroids that were not significant. There was no gross evidence of cancer.

CLINICAL DIAGNOSES

Leiomyoma

Rectocele

Cystocele

Lacerated hypertrophied cervix, with marked endocervicitis

Carcinoma of cervix?

DR. ULFELDER'S DIAGNOSIS

Cystic tumor of left ovary

Cancer of cervix or uterine fundus?

ANATOMICAL DIAGNOSES

Cystadenocarcinoma of left ovary

Leiomyomas of uterus, small

PATHOLOGICAL DISCUSSION

DR. MALLORY When the cyst of the ovary was opened it was found to be lined with innumerable papillary projections. We know that papillary cystic tumors of the ovary are at least potentially malignant. The epithelial cells in this tumor showed evidence of rapid growth and considerable irregularity of staining, and we called it a cystadenocarcinoma. In the other ovary a functioning corpus luteum was found, and the endometrium showed an early secretory stage. There was a moderate amount of functioning ovarian tissue, in spite of the preliminary symptoms of the menopause. We were unable to find evidence of cancer of either the cervix or the fundus of the uterus.

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fifty years ago, and has been to a large degree its guardian since that time

We know Dr Bowers as a former president of the Massachusetts Medical Society, as the secretary for years of the Massachusetts Board of Registration in Medicine, as the managing editor of the *Journal* from 1921 to 1936, but particularly as a physician and friend, loved and respected. Clinton knows him for all this and as the physician who settled in that town over sixty years ago to spend there the most productive years of a long and industrious life in the practice of medicine and in the service of the community. We can all take vicarious pride in the fact that it was as a general practitioner that Dr Bowers received from Harvard University in 1935 the degree of Master of Arts, *honoris causa*.

It is fitting that Clinton's new and modern general hospital should be named after Clinton's foremost physician, for it can thus also stand as a memorial to the spirit of all general practitioners and to the leadership that they have so often given to their various communities. The practice of medicine will change and go forward, and more complicated technics will be developed, but the real value and the true function of the general practitioner will remain indispensable and indisputable.

MASSACHUSETTS MEDICAL SOCIETY

BUREAU OF CLINICAL INFORMATION

All secretaries of various medical groups, such as special societies and alumni associations, are requested to notify the Bureau of Clinical Information regarding scheduled meetings, annual dinners and so forth. If such data are on file, it is hoped that duplication of dates can be avoided.

DEATHS

DENNETT—Alonzo G. Dennett, M.D., of Lowell, died October 11. He was in his ninety-second year. Dr. Dennett received his degree from Rush Medical College in 1883.

His widow and a daughter survive.

McNAMARA—John J. McNamara, M.D., of Lowell, died November 13. He was in his fifty-second year. Dr. McNamara received his degree from Tufts College Medical School in 1923. He was a fellow of the American Medical Association.

His widow and two sons survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR OCTOBER, 1946

RÉSUMÉ

DISEASES	OCTOBER 1946	OCTOBER 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	129	134	46
Chancroid	2	1	2
Chicken pox	478	331	370
Diphtheria	89	15	17
Dog bite	981	742	813
Dysentery, bacillary	6	39	39
German measles	52	46	40
Gonorrhea	413	657	435
Granuloma inguinale	1	0	2
Lymphogranuloma venereum	0	39	0
Malaria	20	3	0
Measles	508	647	401
Meningitis, meningococcal	6	11	11
Meningitis, Pfeiffer bacillus	1	4	1
Meningitis, pneumococcal	2	0	2†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	0	2	0†
Meningitis, other forms	1	0	2†
Meningitis, undetermined	4	3	4†
Mumps	175	326	326
Pneumonia, lobar	73	97	161
Salmonella infections	10	5	6
Scarlet fever	198	372	456
Syphilis	390	436	436
Tuberculosis, pulmonary	239	236	236
Tuberculosis, other forms	19	24	24
Typhoid fever	3	2	4
Undulant fever	3	7	5
Whooping cough	555	640	555

*Made reportable December 1943

†Four-year average

COMMENT

Diseases reported at an incidence above the seven-year median included anterior poliomyelitis, chicken pox, diphtheria, German measles, measles and Salmonella infections.

Diphtheria showed the highest prevalence of any month since 1933 and had an incidence of more than five times that of October, 1945.

Diseases reported below the seven-year median included bacillary dysentery, meningococcal meningitis, mumps and scarlet fever.

Lobar pneumonia had an incidence that was only half that of the seven-year median and that comprises a record low for the month of October.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Arlington, 3; Boston, 8; Blackstone, 2; Brockton, 1; Brookfield, 1; Brookline, 1; Cambridge, 1; Canton, 1; Chelsea, 1; Dracut, 2; Easthampton, 3; Essex, 1; Everett, 2; Fitchburg, 1; Framingham, 2; Franklin, 2; Gardner, 1; Groton, 1; Haverhill, 2; Hopkinton, 1; Holyoke, 1; Lakeville, 1; Leominster, 1; Lowell, 7; Lynn, 1; Malden, 4; Marlboro, 1; Medford, 3; Milford, 1; Milton, 1; Needham, 4; New Bedford, 1; Newton, 10; North Adams, 1; Quincy, 1; Revere, 1; Salem, 1; Scituate, 2; Shelburne, 1; Shrewsbury, 1; Somerville, 2; Southbridge, 3; South Hadley, 1; Stoughton, 2; Walpole, 1; Ware, 2; Wareham, 1; Watertown, 1; Webster, 1; Weston, 1; Winchendon, 1; Worcester, 32; total, 129.

Diphtheria was reported from Arlington, 1; Boston, 21; Brockton, 3; Cambridge, 2; Chelsea, 3; Dartmouth, 1; Everett, 1; Lowell, 3; Lynn, 3; Mansfield, 1; New Bedford, 2; Somerville, 46; Waltham, 1; Worcester, 1; total, 89.

Dysentery, bacillary, was reported from Boston, 1; Lexington (Metropolitan State Hospital), 4; Wrentham (State School), 1; total, 6.

Malaria was reported from Abington, 1; Boston, 5; Dedham, 1; Framingham, 1; Greenfield, 1; New Bedford, 1; North Andover, 3; Saugus, 1; Southboro, 1; Stow, 1; Wellesley, 1; Worcester, 3; total, 20.

Meningitis, meningococcal, was reported from Norwood, 1; Palmer, 1; Salem, 1; Somerville, 1; Springfield, 1; Waltham, 1; total, 6.

Meningitis, Pfeiffer bacillus, was reported from Malden, 1; total, 1.

Meningitis, pneumococcal, was reported from Lunenburg, 1; Marblehead, 1; total, 2.

Meningitis, other forms, was reported from Boston, 1; total, 1.

Meningitis, undetermined, was reported from Hanson, 1, Medford, 1, Norwood, 1, Uxbridge 1, total, 4
 Pottacosis was reported from Cambridge, 1, total, 1
 Salmonella infections were reported from Belmont, 2, Haverhill, 1, Hatfield, 1, Lawrence, 1, Lynn, 2, Peabody, 1, Swampscott, 2, total, 10
 Septic sore throat was reported from Amesbury, 2, Boston, 10, Brookline, 1, Cambridge, 2, Somerville, 1, Williamstown, 6, total, 22
 Tetanus was reported from Ashburnham, 1, Burlington, 1, Fall River, 1, total, 3
 Trichinosis was reported from Boston, 1, Fall River, 1, Mansfield, 1, Medford, 1, total, 4
 Typhoid fever was reported from Boston, 1, North Adams, 1, Wellesey, 1, total, 3
 Typhus fever was reported from Boston, 1, total, 1
 Undulant fever was reported from Bridgewater, 1, Maynard, 1, Millville, 1, total, 3

MISCELLANY

NATIONAL EMERGENCY MEDICAL SERVICE

Edward L. Bortz, M.D., of Philadelphia, chairman of the Committee on National Emergency Medical Service of the American Medical Association, recently announced the mailing of a comprehensive questionnaire to more than 45,000 discharged medical officers of World War II. "Since the results of the questionnaire will serve as a useful guide in preparing for any new national emergency," Dr. Bortz said, "the committee urges all the returning medical officers to express frankly, fully and completely their reaction to military service." The questionnaires were mailed from the headquarters of the American Medical Association during November and should be returned within a month after receipt. The results will be tabulated and analyzed in detail.

Dr. Bortz said that the committee believes that its final analysis and recommendations should cover not only the military services but also other governmental agencies, industry, medical education, research and civilian medical care.

The committee, in so far as possible, has provided check lists in this questionnaire. This makes it possible for the doctor merely to check the proper item and avoid taking the time to write out his answers. Some of the questions, however, will require written explanations. For example: "What important features of training were not sufficiently stressed? What in your opinion should be included in an ideal training program? If there was waste of personnel in your unit, please state how personnel could have been used effectively. What suggestions have you about methods of assignment of medical officers in the event of another military emergency?"

In discussing the questionnaire, Dr. Bortz stressed the desirability of deliberation on the part of every physician in answering the questions. "The objective sought," he said, "can be best attained by careful consideration of each and every question."

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Bibliography of Visual Literature 1939-1944. Compiled by John F. Fulton, M.D., Phebe M. Hoff and Henrietta T. Perkins. Publication No. 11, Historical Library, Yale Medical Library. Prepared by the Committee on Aviation Medicine, Division of Medical Sciences, National Research Council, acting for the Committee on Medical Research Office of Scientific Research and Development, Washington, D.C. 4° cloth, 117 pp. Menasha, Wisconsin. Printed by George Banta Publishing Company, 1945. \$3.00, postpaid.

This bibliography was primarily compiled for military purposes, and therefore a large amount of biochemical material on the aqueous and vitreous humors of the eye was arbitrarily omitted. The special literature on the lens was

also omitted because it is thoroughly covered for the war period in another work. In the section on therapy emphasis is placed on the newer developments both in surgery and chemotherapeutics. Special sections are devoted to the sulfonamides and to penicillin. Trachoma is included because of its importance as a military problem in certain war theaters. Three thousand, three hundred and forty-seven references are cited, and there are indexes of periodicals, authors' names and subjects. This bibliography should be in all medical reference collections, public-health libraries and the libraries of ophthalmologists.

Clinical Parasitology. By Charles F. Craig, M.D., M.A. (hon.), and Ernest C. Faust, M.A., Ph.D., professor of parasitology, Department of Tropical Medicine, Tulane University of Louisiana, New Orleans, consultant to the Secretary of War, Army Epidemiologic Board on Epidemic and Tropical Diseases, consultant, United States Public Health Service, and honorary consultant, Army Medical Library. Fourth edition, thoroughly revised. 8°, cloth, 871 pp., with 305 illustrations and 4 colored plates. Philadelphia: Lea and Febiger, 1945. \$10.00.

The authors in this fourth edition of an authoritative work have completely revised the text and under each important parasite have added a separate topic on pathogenesis. A new chapter has been added on the geographic distribution of parasitic infection. Much new information on preventive techniques has been incorporated throughout the text. A bibliography of thirty-nine pages and indexes of authors and subjects conclude the volume. This work should be in all medical reference collections, public-health libraries and the libraries of physicians interested in tropical diseases.

Fractures of the Jaws. By Robert H. Ivy, M.D., D.D.S., professor of plastic surgery, School of Medicine and Graduate School of Medicine, and of clinical maxillofacial surgery, School of Dentistry, University of Pennsylvania, chief of plastic surgery, Graduate Hospital, consultant in plastic surgery, Children's Hospital, and plastic surgeon, Presbyterian Hospital, Philadelphia, and Lawrence Curtiss, M.D., D.D.S., associate professor of plastic surgery, Graduate School of Medicine, assistant professor of maxillofacial surgery, School of Dentistry, University of Pennsylvania, chief of oral and plastic surgery, Bryn Mawr Hospital, associate in plastic surgery, Presbyterian Hospital, and consultant in plastic surgery, Delaware County Hospital. Third edition, thoroughly revised. 8°, cloth, 174 pp., with 199 illustrations. Philadelphia: Lea and Febiger, 1945. \$4.50.

In this new edition of a popular work a few changes have been made, but the general character of the text remains the same. Several new methods of treatment of fracture of the jaw have been described, and a number of new illustrations have been added to the text.

Acute Injuries of the Head: Their diagnosis, treatment, complications and sequelae. By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.), surgeon in charge, Department of Neurological Surgery, Newcastle General Hospital, neurologic surgeon, Royal Victoria Infirmary, Newcastle-on-Tyne, and Sunderland Royal Infirmary, and consulting neurologic surgeon, Durham County Council, Northumberland County Council, Sunderland Corporation and Gateshead Corporation. With a foreword by Norman M. Dott, M.B., Ch.B. (Ed.), F.R.C.S. (Ed.), lecturer in neurologic surgery, University of Edinburgh, neurologic surgeon, Royal Infirmary, Edinburgh, and Jordanburn Nerve Hospital, Edinburgh, honorary consultant in neurologic surgery to the Army in Scotland, and director in neurology and neurologic surgery, Brain Injuries Unit, Bangour E.M.S. Hospital, near Edinburgh. 8°, cloth, 424 pp., with 201 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$8.50.

This second edition has been revised in the light of knowledge gained from autopsies and clinical experience since the publication of the first edition in 1942. Two chapters on the theory of injury to the brain by the force of rotation and on rehabilitation, as well as new illustrations, have been added to the text.

Hey Groves' Synopsis of Surgery Edited by Cecil P G Wakeley, C.B., D.Sc., F.R.C.S., F.R.S.E., fellow of King's College, London, senior surgeon to King's College Hospital, director of surgical studies and teacher of operative surgery, King's College Hospital Medical School, surgeon, Belgrave Hospital for Children, West End Hospital for Nervous Diseases and Royal Masonic Hospital, consulting surgeon, Maudsley Hospital and Royal Navy, Hunterian professor, Royal College of Surgeons of England, and examiner in surgery, universities of Bristol, Cambridge, Durham and Sheffield. Twelfth edition. 12°, cloth, 632 pp. Baltimore: The Williams and Wilkins Company, 1945. \$6.00.

During the revision of this well known manual, Dr Groves died, and the work was completed by Dr Wakeley. The complete text has been carefully revised and brought up to date. Information on penicillin and the sulfonamides and on modern methods of radium therapy have been incorporated in the text. Some of the older amputations no longer in use have been omitted. This work was first published in 1908, and new editions have been necessitated every few years, speaking well for the popularity of the manual.

The Road to Recovery from Illness. A study of convalescent homes serving New York City. Prepared by Elizabeth G Gardiner and Francisca K Thomas for the Committee on Convalescent Care Practice. 8°, paper, 197 pp. New York: Hospital Council of Greater New York, 1945.

This report embodies the results of a study made on convalescent care in 1941 and 1942 by a special committee representing various New York hospitals and welfare organizations. A survey of the convalescent homes in the New York City area was made by field representatives working for the committee. The study covered the various social and medical aspects of the problem. As a result of the findings, the committee made extensive recommendations concerning co-operation of all agencies in the area, as well as convalescent homes. One of the principal recommendations was that a department of convalescent care be created as a central agency and that all homes serving the population in New York City, regardless of geographical location, should be integrated by this central agency into a community plan for organized medical care. The recommendations for the homes covered medical supervision and health, personnel, policies and plant. The report concludes with various recommendations for the referring agencies.

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This new textbook is the combined effort of a large number of contributors with extensive clinical and teaching experience who are also thoroughly acquainted with the literature of their respective subjects. Of special interest are the articles on endoscopic photography, aviation otolaryngology and chemotherapy.

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NAVAL RESERVE OFFICERS

The attention of reserve medical officers of the United States Navy is invited to the opportunity to perform full-time active duty at one of the major naval air stations of the Naval Air Reserve Training Command or at one of the Naval Air Reserve Training Units.

Officers in the above category who are interested in full-time active duty as a member of the stationkeeper staff at one of these stations or units should initiate letters to the Bureau of Naval Personnel, via the Chief of Naval Air Reserve Training, Naval Air Station, Glenview, Illinois, listing three or four stations at which duty is desired in order of preference. Personnel are desired in the ranks of commander and lieutenant commander.

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Reserve naval flight surgeons who are desirous of affiliating themselves on a part-time basis with either the organized or the volunteer components of the Inactive Reserve, composed of air groups training at one of the Naval Air Stations or Naval Air Reserve Training Units should contact the Commanding Officer of the station or the unit at which the training group is based.

AMERICAN COLLEGE OF SURGEONS

The five-day Clinical Congress of the American College of Surgeons will open in Cleveland on Monday morning, December 16, at 9:30 o'clock. This will be the first annual meeting of the College since 1941. Headquarters will be in the Cleveland Public Auditorium and the Statler and Cleveland hotels, with most of the sessions, except the clinics at the hospitals, being held in the auditorium. The program will include operative and nonoperative clinics, demonstrations, symposiums, panel discussions, forums, medical motion pictures, exhibits, and the twenty-fifth Annual Hospital Standardization Conference, which will convene during the first four days.

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(Notices continued on page xix)

The New England Journal of Medicine

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Volume 235

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TRICHINOSIS

A Review of Cases in Massachusetts from 1936 to 1945

ROBERT E. OBER, M.D.*

QUINCY, MASSACHUSETTS

FOR many years, concerted attempts have been made through the press, magazine articles, popular pamphlets and other channels to impress on the public the danger of contracting trichinosis. Such catch phrases as "Perils of pink pork"¹ and "Why don't we trim trichinosis?"² have been useful in attracting the attention of the general public to the dangers inherent in insufficiently cooked pork. Recently, the death of a Massachusetts physician from a proved trichinella infection indicates that it is difficult even for a highly trained person to recognize improperly cooked pork. Undoubtedly, much pork is consumed daily that harbors trichinae. Nor can it be denied that many cases of human infection are not recognized by the patient or the physician. Hall and Collins,³ in 1937, and Nolan and Bozicevich,⁴ in 1938, routinely examined the diaphragms at autopsy of 1000 consecutive patients in whom the diagnosis of trichinosis had not been considered clinically. They found *Trichinella spiralis* in 174 cases—an incidence of 17.4 per cent. Numerous other investigators have made similar studies of autopsy material in various parts of the country and reported varying results.⁵⁻⁸ Evans⁹ observed *T. spiralis* in 36 per cent of 100 post-mortem cases. There can be no question, therefore, that human infection with trichinae is a relatively frequent condition, probably being present in about 15 per cent of all cases at autopsy.

In Massachusetts, although trichinosis is not reported with great frequency, it cannot be considered a rare disease. In the ten-year period 1936-1945, a total of 287 cases were reported to the Massachusetts Department of Public Health, with death in 7 cases, a mortality of 2 per cent (Table 1). No particular section of the Commonwealth appears to be either immune or subject to an unduly high incidence of the disease, cases have been reported with regularity from all areas (Fig. 1). A total of eighty-one different communities reported one or more cases during this ten-year period. Owing to many factors, however, there can be little doubt

that many more patients were so mildly ill as never to come under medical care. Attention is usually directed to cases occurring in groups or in so-called "epidemic" form, single cases may escape detection.

EPIDEMIOLOGY

Trichinosis is caused by a small parasitic nematode—*T. spiralis*—that was first recognized in 1835 by Owen. Encysted forms of larvae present in infested pork are ordinarily responsible for the origin of the human infection. Human gastric juices destroy the encysting capsule, freeing the contained worms, which then pass on into the duodenum.

TABLE 1 Statistics in Cases of Trichinosis in Massachusetts

YEAR	No. of CASES	No. of DEATHS
1936	36	2
1937	21	1
1938	29	1
1939	14	1
1940	46	2
1941	50	0
1942	19	0
1943	13	0
1944	31	0
1945	28	0
	287	7

and jejunum and mature into adult male and female forms. Copulation ensues, the male worms die and the females bore into the intestinal villi to reach the lymph spaces, where their eggs are deposited. These rapidly hatch to the larval stage and are carried via the thoracic duct to the lung capillaries and heart. The larvae are then disseminated from the heart into the peripheral arterial system and reach the distal capillaries. Sites especially prone to involvement with larvae are the eyelids, diaphragm and striated muscles, especially the gastrocnemius and deltoid. Active migration of the larvae occurs as they pass from the blood vessels and penetrate into muscle fibers. If a larva fails to penetrate a striated muscle fiber, it is

*District health officer, Massachusetts Department of Public Health.

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(Notices continued on page xix)

per cent) involved groups of 2 to 8 people in a total of thirteen separate outbreaks. Pork ingestion was readily traceable in all but 4 cases, the majority of patients admitting frequent exposure to pork meat. In 11 cases there were notations that the pork had been eaten raw—usually because the woman of the household had sampled pork-sausage meat to ascertain its spiciness. Members of the same households who had eaten the cooked product suffered no ill effects. This may possibly account for the fact that 47 of the 70 cases, or 67 per cent, occurred in women. The ages ranged from five to eighty-eight years.

The incubation period was difficult to ascertain in most cases owing to the frequency of pork ingestion. In retrospect, however, 26 cases showed nausea, vomiting, diarrhea and abdominal cramps early in the illness, and a history of pork ingestion within three to five days could be obtained. Most cases, however, showed only symptoms referable to the stage of larval dissemination. There was also difficulty in determining the time lapse, but in 9 cases it was believed with relative certainty that such symptomatology occurred from ten to fourteen days after the ingestion of pork. These figures agree with what may reasonably be anticipated from a knowledge of the life cycle of the trichinae.

During the dissemination stage, the peripheral signs and symptoms were recognized (Table 2)

TABLE 2 Clinical Signs and Symptoms in Disseminative Stage of Trichinosis

Sign or Symptom	No. of Cases
Temperature elevation*	67
Malaise	52
Edema of eyelids	47
Conjunctival involvement	10
Facial edema	19
Muscle pains	
Generalized	27
In legs	15
In upper extremities	2
In neck	2
In back	4

*Includes temperatures of 99 to 105°F, with an average of 101.3°F

Edema of the eyelids was a predominant feature in 47 cases, or 67 per cent. Conjunctival involvement included either edema or hemorrhage into the conjunctiva, or was recorded as "conjunctivitis." Only 1 case occurred in which concomitant edema of the eyelids did not exist. Facial edema was prominent in 19 cases, but in only 2 was edema of the eyelids absent. Muscle pains were relatively prevalent, being prominent in a total of 51 cases (71 per cent). Generalized muscular pains were prominent in 27 cases, or 39 per cent. The legs were specifically mentioned in 15 cases, with frequent notations specifying the gastrocnemius muscles or calves in contradistinction to the upper extremities, in which the arms and shoulders were both mentioned as the sites of discomfort.

Less frequent findings were those indicating pulmonary involvement, chest consolidation being reported in 1 case, chest pains in 4 and cough in 3. Cervical adenitis was mentioned once, as was splenomegaly. Abdominal distention and edema of the extremities were each described twice. Blurring of vision, profuse perspiration and skin rash were described in 4 cases, the last being generalized in 2 and confined to the chest in 1 and to the lower extremities in 1.

Laboratory examinations included white-cell counts, differential counts for eosinophils, precipitin tests, skin tests and muscle biopsies. White-cell counts were reported from 5000 to 26,000, with an overall average of 14,500 and individual cases showing fluctuations from 5000 to 19,000. Eosinophilia was characterized as "elevated" in 16 cases, whereas in the remainder the eosinophil count was specifically recorded in figures ranging from 6 to 85 per cent, individual cases showed fluctuations of as much as 55 per cent on repeated counts. The count was 32.5 per cent as an overall average and was 10 per cent or less in only 5 cases.

Precipitin tests were reported in a total of 16 cases, of which 13 were positive. Skin tests were done in 15 cases, with positive readings in 9. Most of the negative readings, however, were single tests, all done within four or five days of the onset of the symptoms. Undoubtedly, repeated tests would have resulted in a greater number of positive readings.

Muscle biopsy, which was made in 7 cases, was reported negative in 3, positive in 3 and as showing "interstitial myositis" in 1.

The establishment of the diagnosis of trichinosis is ordinarily done in the stage of larval dissemination. Fever, malaise, muscular pain and edema of the orbital region are the most frequent and significant findings. Eosinophilia, often of a high degree, points to the diagnosis. Precipitin and skin tests, together with muscle biopsy, offer a positive diagnosis but are subject to certain limitations and interpretations.

A definite diagnosis is rarely made in the early stages. Reported earlier diagnoses in the 70 cases described above had included "grippe," acute nephritis, chronic rheumatic fever, pyelonephritis, gastroenteritis, staphylococcal infection, food poisoning and poliomyelitis. Pepper³⁸ mentions typhoid fever, angioneurotic edema, meningitis, tetanus and acute sinusitis as being possibilities in differential diagnosis.

PREVENTION

Since the therapy of trichinosis has not been highly satisfactory,³⁷ the main interest revolves about the prevention of the disease. Inspection of meat by federal agents does not mean that any meat or meat product can be guaranteed to be free of trichinae. Because of the technical difficulties involved, meat cannot be investigated for *T. spiralis*.

quickly surrounded by a focus of acute inflammatory exudate and destroyed. Since the adult worms in the intestines live about four or five weeks, they may produce larvae for a prolonged period. With death, the adult worms are discharged in the feces. Larvae that reach a locus within a muscle fiber grow somewhat in length, assume a spiral form and become encysted, remaining alive and capable of development for many years. Many such cysts become calcified, and the contained larvae tend to die after a number of years.¹⁰

Porcine infestations undergo the same course. Rats have also been mentioned frequently as sources of *T. spiralis*, although their exact role in the transmission seems to be somewhat obscure.¹¹ Those who

and are followed by a period of muscular aching, pain and tenderness, chills, a temperature up to 105° F, cough, edema of the eyelids and skin rash. Not infrequently, signs and symptoms of pulmonary,¹⁹ cardiac²⁰⁻²² and central-nervous-system²⁴⁻²⁸ involvement are found. Undoubtedly, Augustine's¹³ observations that the inflammatory exudate surrounding the larvae reaching the brain, heart and pancreas destroys the parasites explains why such involvement is only transient. A similar action, he believes, accounts for the inability of the trichinae to pass across the placenta and involve the fetus in utero.

The period of peripheral symptomatology lasts as long as the adult worm is producing eggs—five to seven weeks. Death of patients affected occurs most frequently from the third to the sixth week. Although recovery is usually complete, vague rheumatic pains may persist for about a year.¹⁵

LABORATORY FINDINGS

The most frequent laboratory aid is the eosinophil count. Trichinosis almost invariably causes a relative and absolute eosinophilia. This fact, which has long been recognized as one of the most reliable signs of trichinosis,²⁹⁻³² is not in itself diagnostic but merely presumptive, other laboratory tests being necessary for absolute diagnosis.

The precipitin test, which is usually done by the National Institute of Health at Bethesda, Maryland, is highly sensitive. Unfortunately, it has several drawbacks. Early in the illness it may be negative, three or four weeks often being required before the precipitin titer is elevated. Repeated tests, however, showing a rising titer during the illness as well as the convalescence, are diagnostic.³³ This high titer may persist for years, thus obscuring the diagnosis of some other unrelated illness.³⁴

The skin test is of value if there is first an initial negative response to intradermal injection of the antigen, followed at a later date by a positive reaction, or if a delayed positive reaction is followed by an immediate positive one.³⁴ Immediate positive skin tests may represent an infection with *T. spiralis* as long as three years previously.³⁵

Muscle biopsy, if positive, makes diagnosis certain, but is often objectionable to the patient, takes time and frequently yields negative results.

Dammin³⁴ suggests utilizing the technic of Herick and Janeway³⁶ for the demonstration of larvae in the arterial blood. Although this procedure seems to offer a positive diagnostic aid, other references to its use have not appeared in the recent literature.³⁷

CASES IN MASSACHUSETTS

A review of the 287 reported cases of trichinosis in Massachusetts reveals 70 in which sufficient information was available to the Department of Public Health for evaluation of epidemiologic, clinical and laboratory data. Of these, 39 (approximately 55

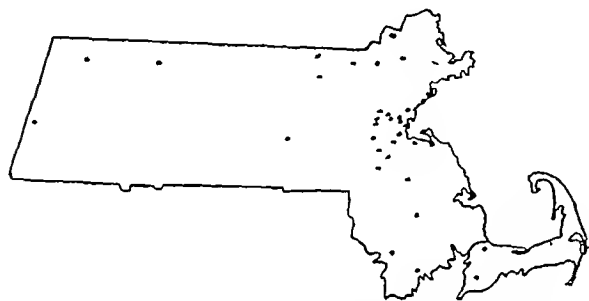


FIGURE 1 Massachusetts Communities Reporting Trichinosis during 1936-1945

have watched rats feeding in the troughs from which swine are fed can readily realize their importance in this respect. In addition, *T. spiralis* has been described in foxes, badgers, martins, raccoons and so forth,¹² although no epidemiologic significance can be ascribed to this observation. Undoubtedly, the porcine reservoir is the basis for the organism found in rats, swine and human beings. Infested meat scraps fed to pigs in the form of garbage are undoubtedly the chief sources of porcine and rodent infestation.¹⁸ Unusual sources, such as that traced to bear meat by Westphal,¹⁴ play a relatively small part.

SYMPTOMATOLOGY

During the course of the life cycle of *T. spiralis* in human beings, certain signs and symptoms become manifest with each phase of larval development. Ordinarily, cases of great clinical severity can be attributed to an initial ingestion of large numbers of trichinella cysts with their subsequent development.¹⁶ The first symptoms are generally gastrointestinal, consisting of nausea, vomiting, abdominal pain and diarrhea. Recurrent infections may result in immunity to the adult worms and in their elimination from the intestinal tract by active diarrhea shortly after ingestion, as the investigations of McCoy^{16, 17} and Roth¹⁸ demonstrated in experimental studies on rats and guinea pigs. Gastrointestinal symptoms last three to five days

TROPICAL DISEASES IN VETERANS OF WORLD WAR II*

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SINCE the cessation of hostilities, some ten million soldiers, sailors and marines have returned from overseas and resumed civilian life. Because a significant percentage served in areas notorious for the prevalence of tropical and exotic diseases, a serious concern quite justifiably exists regarding the possible effects on civilian public health and on civilian medical practice in general.

Butler and Saperó,¹ in 1945, analyzed the possibilities of new tropical diseases being introduced into the United States and stated that, during the two-year period 1943-1944, many thousands of servicemen who had acquired tropical diseases overseas had already returned and that no new foci of tropical disease had appeared in civilian communities in this country as a result. In spite of the great influx of patients suffering from recurrent malaria, the opinion was expressed that it was unlikely that carriers of this disease would cause a significant increase in the total incidence of malaria in the United States or that there would be an appreciable occurrence of malaria in areas previously free of the disease. The fact was emphasized, however, that the South Pacific strain of vivax malaria was more virulent and seriously disabling than any prevalent in this country. Concern was expressed that if this strain became established in the United States, it would greatly aggravate the malaria problem.

None of the other tropical diseases seemed to present any discernible hazard. Viewing the problem broadly, it was concluded that there appeared little cause for alarm regarding postwar morbidity from tropical diseases newly introduced into civilian communities.

It is now possible to review the estimate of the situation as it appeared in November, 1944, in the light of further experience. Since that time, several million members of the armed forces have returned to civilian life, and specific data on tropical diseases acquired by the armed forces during the entire war period have become available. Although the conclusions derived from the earlier analysis remain substantially the same, a clearer definition of the effects that tropical diseases may exert on postwar civilian life is now possible.

DISEASES OF MAJOR OCCURRENCE

Dysentery and diarrhea, malaria, infectious hepatitis and dengue, in respective order of frequency,

constituted the tropical diseases of major occurrence in some 11,300,000 persons who served overseas from 1942 to 1945, inclusive (Table I). As in almost every war in the past, the dysenteries, which occurred in approximately 6700 out of each 100,000 men, headed the list of the tropical diseases in World War II. Malaria, as might have been guessed, ranked second in frequency, with a rate of 5100 per

TABLE I Tropical Diseases in the Armed Forces, 1942-1945

DISEASE	ARMY	NAVY	TOTAL	APPROXIMATE RATE PER 100,000
Dysentery and diarrhea	523,449	231,400*	756,849	6700
Malaria	462,070	110,850	572,950	5100
Infectious hepatitis	172,000	19,774	191,774	1700
Dengue	84,100	37,503	121,603	1100
Hookworm	13,000*	6,943	19,943	180
Filariasis (Bancrofti)	2,150	11,859	14,000	120
Sandfly fever	12,400	234	12,634	110
Typhus, scrub	6,861*	560	7,421	86
Dysentery, amebic	3,051*	1,453	4,504	40
Schistosomiasis	1,616	36	1,672	15
Typhus, endemic	491*	402	893	8
Leishmaniasis	346	15	361	3.00
Relapsing fever	220	19	239	2.00
Smallpox	116	9	125	1.00
Typhus, epidemic	61*	2*	63	.60
Cholera	14	0	14	.10
Trypanosomiasis	2	3	5	.04
Plague	0	0	0	0
Yellow fever	0	0	0	0
Leprosy	0	0	0	0

*Estimated — all other data derived from official sources and still in process of compilation and editing.

100,000. A surprising finding, however, was the occurrence of infectious hepatitis as the third disease on the list, with an approximate rate of 1700 per 100,000. The fourth disease — dengue — had a rate of 1100 per 100,000.

Dengue

In evaluating the four diseases of most frequent occurrence in the light of their potential postwar effect on civilian life, it can be said that dengue at least presents no problem. There has been no case in which this disease, once widely prevalent in the United States, has been reintroduced, nor are there chronic sequelae that will require medical care during the postwar period.

Malaria

The status of malaria is more difficult to evaluate. It may be said, however, that the vast majority of malarial infections contracted during the war have run their course. Military hospitals, overcrowded in 1943 with cases of malaria, now are treating only an occasional patient for the disease. Fortunately, the syndrome of so-called "malaria cachexia" has occurred rarely, if at all, even in the more persistent

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routinely or completely. Microscopic examination of pork is highly unreliable and is not utilized as a routine measure. It must also be realized that only 60 per cent of the hogs slaughtered in this country are federally inspected.³⁹ Attempts have been made by various state legislatures to compel hog breeders feeding garbage to hogs to steam cook all such material. Although this procedure undeniably destroys parasites present in pork scraps,⁴⁰ the time and expense involved do not make this practice popular. In Canada, however, where such cooking is governed by statute, the reported number of cases per 100,000 population is one twelfth that in the United States. Gould⁴¹ suggests a newer method of control that may eventually prove more acceptable. Freezing of pork at a temperature of 5°F for twenty days in sections 15 cm or less in thickness destroys trichinae. Raw pork kept at 0°F for seventy-two hours is rendered free of living parasites, and ground pork preserved at the same temperature is freed of *T. spiralis* in a few minutes. If this method is generally adopted and all pork refrigerated at the required temperatures, it is entirely conceivable that a generalized decrease in trichinosis can be anticipated. The growing popularity of deep-freeze cabinets in the home may be expected to contribute to this end.

Ultimately, however, the control of trichinosis is the responsibility of the consumer. Uncooked pork, regardless of the source and regardless of whether it has been inspected by federal, state or city authorities, must be considered unsafe unless properly cooked. Undoubtedly, much of this type of pork is perfectly safe, but the added factor of proper cooking is of sufficient value to be advised routinely. Ordinarily, the main sources of difficulty are not in eating the various pork products raw but in cooking them to an insufficient degree. Cooking must remove all traces of pink color from the meat and leave it a dull white. Then, and only then, can pork be considered noninfectious for *T. spiralis*.

SUMMARY

Of 287 cases of trichinosis reported in Massachusetts from 1936 to 1945, a total of 70 are reviewed for epidemiologic, clinical and laboratory data of significance and compared with the accepted clinical picture of the disease.

The clinical findings most frequently noted were fever, malaise, orbital edema and muscle pains. Eosinophilia was the most constant laboratory finding but must not be considered diagnostic in itself.

The control of trichinosis, in the final analysis, can be guaranteed only by the complete cooking of all pork and pork products. New deep-freezing methods may soon be expected to aid in the lowering of infectivity of pork.

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had jaundice should be taken, and when the history is positive, special studies to reveal either latent or overt hepatic dysfunction should be made

DISEASES OF LESSER BUT SIGNIFICANT OCCURRENCE

Whereas Table 1 lists in the first group four diseases whose numerical occurrence was in the hundred thousands, the second group involved at the most less than one tenth as many patients

The reported occurrence of 20,000 cases of hookworm undoubtedly represents a small fraction of the actual number of patients who acquired this infection. Prewar Army and Navy surveys indicated an incidence of *Necator americanus* infections in from 5 to 10 per cent of recruits from the South. Postwar surveys of personnel who have served overseas show by comparison that a significant number of new infections have been acquired in endemic areas overseas. Fortunately, infections sufficiently heavy to cause serious clinical manifestations have not occurred frequently. In most of the hookworm-positive cases the infection is light, and the worms are lost spontaneously.

Whereas the over-all problem from a clinical standpoint appears of little importance, the fact that many of these men have acquired infections with *Ancylostoma duodenale* is a matter of some concern. *A. duodenale* is not at present found in the endemic hookworm areas of the United States. Thus, there is a possibility that returning servicemen, in unsanitated areas, will cause the introduction of this species, which is considered more pathogenic than *N. americanus*.

Careful studies by both the Army and the Navy now permit the statement that few, if any, permanent disabilities will result from filariasis. Furthermore, repeated blood studies have shown the occurrence of microfilaria to be exceedingly rare. Since transmission is dependent on their presence in the blood stream, this suggests that filariasis is unlikely to become established in the United States.

Neither endemic nor scrub typhus appears likely to present a postwar problem. Of the total of 893 cases of endemic typhus, practically all were actually acquired in the United States, this is in contrast to almost all the other diseases, in which the vast majority of cases were acquired overseas. Regarding cases of scrub typhus, most of which were acquired in the Southwest Pacific or in the China or India-Burma Theater, the absence of a suitable vector in the United States and of acute cases as sources of infection renders postwar dissemination improbable. For the same reason sandfly fever can likewise be said to have no particular postwar importance. It is believed that as a result of careful search among exposed groups practically all cases of schistosomiasis have been diagnosed and given intensive curative treatment.

The most serious disease in this group in all probability is amebic dysentery. It can be said with

certainty that the actual number of infections far exceeds those reported. The problem is not one of introduction or dissemination, for it is well known that the causative organism, *Endamoeba histolytica*, is already prevalent in 10 per cent of the population of the United States. The difficulties are clinical, being due to latency, chronicity and, most of all, the frequently obscure symptoms that mitigate the chances of recognition of amebic infections.

DISEASES RARELY ENCOUNTERED

In contrast to the first two groups of diseases, the third group in Table 1 has been compiled principally to show certain tropical diseases that, although they might have been expected to occur fairly often, were actually acquired rarely or not at all.

Of great interest is the fact that the wartime prevalence of the five quarantinable diseases—smallpox, cholera, plague, epidemic typhus and yellow fever—was insignificant when one realizes the large numbers of men and women operating in areas in which an appreciable hazard of acquiring these diseases existed.

Of importance, however, is the occurrence of 125 cases of smallpox. In every case in which full information was available, it was found that the fault lay in failure to obtain successful vaccination. There has not been a single case that would lead to suspicion that American-produced vaccine failed to protect even against the extremely virulent Oriental strains of smallpox.

Despite the relative rarity with which smallpox occurred, this disease has led to outbreaks in civilian communities as a result of introduction by members of the armed forces. Two localized epidemics have been reported. In San Francisco, 6 cases that appeared in civilians were assumed to be traceable to a case in a soldier who arrived in the acute stage of the disease from overseas by airplane. More serious is the recent epidemic in Seattle, in which up to the present, there have been some 59 cases, with 16 deaths, originally traceable to a soldier who arrived by surface vessel.

Even prior to the introduction of smallpox into these two civilian communities, its first occurrence in servicemen overseas was followed by an intensive program of revaccination of all exposed personnel in both the Army and Navy. Tightening of aircraft and ship quarantine, as a further safeguard, was instituted. Quarantine officers of the United States Public Health Service, working in close collaboration with quarantine officers of the armed forces, are maintaining close surveillance of all men returning from overseas to prevent, so far as possible, any further epidemics of quarantinable disease, such as those in San Francisco and Seattle.

The epidemics of smallpox on the West Coast forecast a potential hazard of considerable future public-health significance. Civilian air travel from

infections. Another point of practical postwar importance to physicians is that such cases of recurrent malaria as may be encountered will almost without exception be those of the benign tertian type. Quartan malaria, a disease that is apt to persist for many years, has been acquired only by an exceedingly small number of service personnel. Infections of malignant tertian malaria, although not of infrequent occurrence overseas, are of short duration, readily respond to treatment and, unlike benign tertian infections, do not tend to recur. As a result, malignant tertian infections have not been encountered in servicemen returning from overseas, except in the few who have come directly to this country after recent exposure in a malarious area.

In spite of previously expressed concern regarding the introduction of a new strain of malaria, no evidence has been forthcoming that the more seriously disabling South Pacific strain of *Plasmodium vivax* has become established in this country. It is not possible, however, to be at all certain on this point, since considerable time will elapse before its establishment is apt to be recognized. If establishment occurs, not only will cases infected with this exotic strain have a severer clinical course but also the relapses will be more frequent than those of the indigenous strain of benign tertian malaria. Of even greater import, the American Negro, although relatively refractory to the *P. vivax* strain in the United States, appears as susceptible as nonimmune Whites to the South Pacific strain. This means that the Negro population of the South may suffer serious consequences if the South Pacific strain becomes established in this country.

So far as it is known, there is only one report of a case in which malaria transmission appeared in the United States in an area previously free of the disease. In 1945 Osgood² described 2 primary cases of malaria in civilians in Oregon in an area where anophelines capable of transmitting the disease were found, and where a returned soldier was identified as a carrier and the probable source of the disease.

Although malaria in men returning from overseas is becoming relatively rare, and the peak of opportunity for introduction into new areas thus appears to have passed, it is of interest to note that Watson³ recently demonstrated that *Anopheles quadrimaculatus*, the important vector of malaria in the United States, is capable of transmitting the South Pacific strain of *P. vivax* malaria. Thus, a distinct hazard still exists and warrants maximal measures of anopheline control.

Bacillary Dysentery

Fortunately the vast majority of cases of bacillary dysentery and diarrhea encountered in the armed forces have been mild and of short duration. That chronic disabilities from dysentery are not likely

to present a major postwar problem is evident from the small number of patients with chronic dysentery now under treatment in military hospitals. Special epidemiologic reports on Navy personnel indicate that few persistent carriers have resulted from wartime-acquired dysentery. Although this suggests that overseas veterans as a group probably not present a particularly dangerous carrier problem, careful public-health scrutiny will be required to ascertain whether such a view proves to be true in practice.

Infectious Hepatitis

Of the four most frequent diseases, infectious hepatitis appears by far the likeliest to lead to significant postwar repercussions.

The total figure for the armed forces includes hepatitis transmitted in two distinct ways. One method of transmission resulted in epidemic outbreaks usually associated with a widespread prevalence of dysentery. The mechanism of transmission in these outbreaks, although not definitely established, is assumed to be similar to that in dysentery transmission. In addition, the figures include an indeterminate but significant number of cases of so-called "homologous serum jaundice." These cases followed the therapeutic use of blood or blood products unknowingly obtained from donors harboring the hepatitis virus. For example, of the total of 172,000 cases in the Army, a large number were jaundice infections that resulted from the program of yellow-fever vaccination, in which certain lots of vaccine, to which human serum had been added, were contaminated with the jaundice-producing virus. Other cases followed the use of whole blood or plasma obtained from donors who were probably experiencing unrecognized subclinical attacks. The injection of pooled lots of convalescent serum into a series of patients is especially hazardous. In this procedure, the chance of including a donor who may be carrying the virus is increased, and since there are multiple recipients, a large number of cases of hepatitis may follow.

The essential postwar danger to the civilian population is that the high wartime prevalence of hepatitis in the armed forces may lead to an increasing civilian prevalence by passage of the icterogenic virus in the therapeutic use of blood. Fortunately, there is already keen appreciation of this problem, and active research is underway to set up necessary safeguards. Until safe methods can be devised, physicians must recognize and evaluate the danger involved and weigh this danger in the individual case against the prospective therapeutic advantage.

Another point of practical significance in the large-scale occurrence of hepatitis in the armed forces is the fact that at least a small percentage of patients may develop cirrhosis. In the medical care of veterans, a careful history to determine if a patient has

TABLE 1 *Data in 10 Cases of Tetanus among German Prisoners*

Case No.	INJURY	INCUBATION PERIOD	SPECIFIC PROPHYLAXIS	OPERATIVE TREATMENT	ANTITOXIN THERAPY		CHEMOTHERAPY AFTER DIAGNOSIS	TRANSFUSION	COMPLICATIONS	RESULT
					INTRAVENOUS	INTRAMUSCULAR				
		days			A units	A units				
1	Gushot wound of right thigh and compound fracture of femur	6	None recorded	Redebridement	40 000	30 000	None recorded	500 cc of blood	None recorded	Death 24 hours after beginning of treatment
2	Penetrating wound of hand and compound fracture of metacarpal	8	1500 units of antitoxin 5 days after injury	Amputation of left hand above wrist	20 000	50 000	None recorded	None recorded	High temperature and severe spasms	Death
3	Severe burns of face, hand, thigh and knee	10	0.5 cc. of toxoid 1 day after injury	None	20 000	60 000	1 gm. of sulfadiazine every 4 hours and 20 000 units of penicillin every 3 hours	None recorded	Pulmonary atelectasis, pulmonary edema, pleural effusion and anemia (red cell count of 1,500 000)	Death on third day of treatment
4	Gushot wound of right forearm, compound fracture of right ulna, penetrating wound of chest and laceration of scalp	14	1500 units of antitoxin 8 days after injury	Amputation of right arm above elbow	40 000	100 000	23 gm. of sulfadiazine and 1 000 000 units of penicillin	750 cc of plasma and 2000 cc of blood	Atelectasis of right lung, fecal impaction and oliguria	Recovery
5*	Compound fracture of metacarpal and six other penetrating and lacerating wounds	22	1500 units of antitoxin on day of injury	Redebridement of all wounds	30 000	140 000	640 000 units of penicillin	1500 cc of blood	Local tetanus near one wound in leg, mild pulmonary atelectasis and serum sickness	Recovery
6	Compound fracture of left tibia	5	1 cc. of toxoid on day of injury and 3000 units of antitoxin 4 days after injury	Amputation of left lower leg	30 000	110 000	44 gm. of sulfadiazine and 1 000 000 units of penicillin	500 cc of plasma and 4000 cc. of blood	Severe atelectasis of both lungs with pneumonia, laryngospasm, alkalotic tetany(?) and oliguria	Recovery
7	Lacerating wound of right thigh, with foreign body	11	0.5 cc. of toxoid on day of injury and 1500 units of antitoxin 9 days after injury	Redebridement		120 000	34 gm. of sulfadiazine and 640 000 units of penicillin	None recorded	Oliguria, spasms of bladder sphincters and mild pulmonary atelectasis	Recovery
8†	Multiple lacerating wound of left buttock, thigh and right leg and compound fractures of toes of left foot	10	1500 units of antitoxin 6 days after injury	Redebridement	10 000	110 000	12 gm. of sulfadiazine and 1 120 000 units of penicillin	1500 cc. of blood	None recorded	Recovery
9	Severe burns of face, arms and neck	8	750 units of antitoxin 5 days after injury	Redebridement and removal of powder particles	40 000	110 000	40.5 gm. of sulfadiazine and 1 280 000 units of penicillin	500 cc. of plasma and 5300 cc. of blood	Bleeding from debrided areas	Recovery
10	Compound fracture of tibia and fibula and two penetrating wounds of left thigh, with foreign body	10	1500 units of antitoxin 1 day after injury	Redebridement		180 000	45 gm. of sulfadiazine and 980 000 units of penicillin	500 cc. of plasma and 2000 cc. of blood	Abdominal distention, bladder-sphincter spasms, pulmonary atelectasis, severe (?) tetanus) spasm resulting in death and extensive pulmonary atelectasis with intrapulmonary hemorrhages found at autopsy	Death on seventh day of treatment

*This patient had generalized tetanus, with especially severe local tetanus in one leg.

†Symptoms began as local tetanus in one leg for 4 or 5 days and muscle spasm finally spread to whole body.

the Orient and other endemic areas may be expected to occur in the future on an ever-increasing scale. Although vaccination will be required in international travel, improperly vaccinated persons may arrive while in the incubation period of the disease and may travel far inland before recognizable symptoms occur. The only foolproof countermeasure is for civilian communities to maintain a high level of group immunity by sustained and comprehensive vaccination programs.

SUMMARY

Data regarding the occurrence of tropical diseases in the armed forces during the wartime period of 1942 to 1945 inclusive are presented. Of the diseases usually termed "tropical," those of a major occurrence in men who served overseas, in order of frequency, were dysentery, malaria, infectious hepatitis and dengue. The incidence of all other tropical diseases contracted during this period was remarkably small considering what had been anticipated in view of overseas exposure in highly endemic areas.

The points of greatest postwar significance to civilian public-health and medical practice in general appear to be the following:

There is small likelihood, despite the high wartime prevalence of dysentery, that chronic disability will occur in any large number of veterans or that

there will be a significant spread of bacillary infections in civilian communities.

The end of the once serious problem of malaria appears to be in sight. The vast majority of recurring malarial infections have expended themselves. Although significant spread of the disease in civilian communities appears not to have occurred to date, the improved situation still does not warrant a relaxation of control efforts.

The large-scale occurrence of infectious hepatitis during wartime may result in postwar problems of continuing gravity. The essential danger is dissemination incident to the therapeutic use of blood and blood derivatives.

Intensive measures have been undertaken by the armed forces to prevent the further occurrence of smallpox epidemics such as have already appeared in two civilian communities. Modern rapid civilian air travel presents a future danger of smallpox introduction against which the surest countermeasure for civilian communities is comprehensive smallpox vaccination.

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NOTES ON THE TREATMENT OF TETANUS

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BOSTON AND PHILADELPHIA

PROPHYLAXIS against tetanus by means of active immunization with tetanus toxoid reduced the incidence of this disease among wounded United States Army personnel to a low figure. Only 1 case of tetanus had been reported in the European Theater by February 1, 1945. In the German Army, however, active immunization by means of toxoid was given only to those who stood the greatest chance of being wounded far from their own lines, such as members of the *Luftwaffe* and paratroops. The great mass of the German Army received no active immunization and had to depend for protection on the passive immunity supplied by tetanus antitoxin administered at the time of wounding. As a result, tetanus was frequently encountered in German prisoner casualties treated in United States military hospitals. Since the rarity of the disease among American soldiers has denied many American physicians the opportunity of dealing personally

with its many problems, it seems worthwhile to present our experience gained in the care of 10 cases of tetanus that developed among the 3507 sick and wounded German prisoners treated at an overseas station hospital between September, 1944, and March, 1945. A summary of the clinical course of each of these patients is presented in Table 1. Some of the important points regarding the clinical problems and therapeutic management are discussed below.

Incubation Period

The incubation periods ranged from five to twenty-two days, with an average of slightly over ten days. Although in this series no correlation could be made between the length of the incubation period and the mortality, because of the variable factor of antitoxin administration before the onset of the disease, it is interesting that all the deaths occurred with incubation periods of ten days or less. It should be noted, however, that 3 of the 6 survivors had short incubation periods—ten, eight and five days, respectively.

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the differential diagnoses to be considered include mumps, peritonsillar abscess, affections of the temporomandibular joint, trismus following tooth extraction, a wound involving the mouth and jaws directly, and tetanus. The presence of the first one of these conditions may be readily determined. In their absence tetanus must be considered the diagnosis. In addition to lockjaw, the patient will probably show tenseness of the face muscles producing the risus sardonicus, as well as increased tonus of the sternocleidomastoid muscles, which makes them easily palpable even when the patient's head is lying relaxed on his pillow. Continuous spasm and rigidity of the abdominal muscles may already have developed or may soon follow. Usually accompanying these signs are fever, profuse sweating, extreme mental apprehension and beginning difficulties in swallowing and expectorating. The muscle spasm and rigidity gradually spread over the whole body, opisthotonos develops and the patient becomes "as stiff as a wooden Indian." Sudden, severe local spasms or generalized convulsions, superimposed on the continuous muscle rigidity, are caused by such external stimuli as noise, changing the bed or dressing the wound.

The onset of tetanus beginning with local symptoms is characterized by increasing irritability of the muscles in one part of the body—usually in the vicinity of a wound—that develops several days after injury. At first, the patient may complain only of painful intermittent cramps in the involved region. Within a day or so the cramps become more and more frequent and are brought on by weak stimuli, such as merely touching the bedclothes or exposing the patient to a cold draught. Gradually, the whole group of muscles in the neighborhood of the wound shows continuous spasm. These muscles are tense and firm at all times, and merely touching them produces a severe spasm of the whole extremity and possibly of the contralateral extremity as well. Following this, generalized tetanus often develops. It is necessary and difficult to differentiate this form of tetanus from local muscle spasm resulting from direct injury to muscle or nerve. In general, spasm resulting from direct injury may be expected to decrease a few days after the wound, whereas that from tetanus usually begins only after the first few days have passed. In doubtful cases the condition should be treated as if it were tetanus.

The initial symptom in one patient (Case 8) was local spasm in one leg that was not diagnosed for four days. Even after treatment was started, signs of generalized tetanus of a mild sort developed. One patient with generalized tetanus (Case 5), who had had six major wounds débrided at the onset of symptoms, showed maximum muscular spasm in the vicinity of a seventh wound, which had not been débrided because of its apparent insignificance. Because of the persistence of this local irritability,

débridement was subsequently performed, and a dirty piece of uniform was removed from this small but deep wound.

Bacteriology

Little help in the practical management of a case of tetanus can be obtained from culture of the wounds for *Cl. tetani*. In many war wounds, bacilli are found that resemble *Cl. tetani* morphologically but are nonpathogenic organisms. Furthermore, proved *Cl. tetani* can be cultured from about 20 per cent of all war wounds in the absence of clinical tetanus. The isolation and identification of the organism take too long to be of help in early diagnosis.

Treatment

Before the treatment of a case of tetanus is begun, it is well for the physician to have a clear conception of the magnitude, complexity and duration of the problem confronting him. The patient will usually have an operation under anesthesia for redébridement of his wound. He will be seriously ill for ten days or two weeks and almost completely helpless. In addition to the pain, spasms, muscular rigidity and mental apprehension produced by tetanus, the patient usually suffers from a serious wound, which in itself requires expert surgical or orthopedic attention and which may already have disturbed the bodily economy by means of infection and loss of protein, hemoglobin and electrolytes. As a result, the fluid, electrolyte, caloric and protein requirements are excessive, and yet the patient cannot eat and drink in the ordinary way. He may be incontinent of urine and feces. He is subject to all the allergic reactions consequent to the administration of antitoxin, as well as to dangerous complications at every turn that may demand immediate intervention. In view of these facts, adequate preparation must be made from the beginning to meet successfully the difficulties ahead.

In the first place, special attendants must be selected to care for this patient, and this patient alone, day and night. They should be the most reliable, observant and steady personnel available. Secondly, a suitable place, apart from other patients and visitors, should be selected. It is best to have one room for the patient and another for the attendant. These rooms should be equipped with all the materials necessary for the care of the patient, so that they form a unit in which the personnel may function free from the delays of ordinary hospital procedure.

Having arranged for suitable personnel and a properly equipped place for the care of the patient, the physician should outline a definite schedule of treatment on an hourly timetable. Many treatments, medications, dressings and procedures of one sort or another should be scheduled in groups

Mortality

Of the 10 patients treated, 4 died. The first 3 patients died within three or four days of the onset of symptoms, the other patient died suddenly on the seventh day of treatment, at a time when he appeared to be recovering. Other factors besides the length of the incubation period undoubtedly played a role in the successful outcome of those who recovered. Chief among these, in our opinion, was the factor of increased experience in handling the problem gained during treatment of the first 3 fatal cases. Another factor may well have been the larger amounts of antitoxin given to those who recovered.

Prophylaxis

Data covering the time, type and amount of specific prophylaxis were available in 9 of the 10 cases. In none of these had the prophylaxis been satisfactory. The rules governing proper prophylaxis are as follows: a person who has already been actively immunized by tetanus toxoid should receive a booster dose of 1 cc. at the time of injury — it is useless to give a so-called "wound dose" of toxoid to a person who has not been previously actively immunized, because the development of antibodies from the first dose is too little and too late to prevent the occurrence of the disease, a patient who has not been actively immunized must be given passive immunity by means of tetanus antitoxin at the time of injury. Experience in World War I demonstrated that the amount of antitoxin should be 1500 (American) units and that it should be given, if possible, on the day of the wound and repeated at weekly intervals for a total of three doses. The passive immunity created by the administration of one dose of 1500 units of antitoxin is protective for only seven to fourteen days, and unless this dose is repeated, as recommended above, tetanus develops in a certain number of cases. In the patients studied by us, the following deviations from these recommended procedures were noted: in Case 2 a dose of 1500 units of antitoxin was given, but not until the fifth day after injury, and tetanus developed on the eighth day, in Case 3, instead of antitoxin, 0.5 cc. of toxoid was given on the day after the wound was received, and tetanus developed on the tenth day, in Case 4 a total of 1500 units of antitoxin was given, but not until the eighth day after wounding, and tetanus developed on the fourteenth day, in Case 5 a dose of 1500 units of antitoxin given on the first day was not repeated, and tetanus developed on the twenty-second day, in Case 6, instead of antitoxin, 1 cc. of toxoid was given on the day of injury, and tetanus developed on the fifth day in spite of 3000 units of antitoxin finally given on the fourth day, in Case 7, instead of antitoxin, 1 cc. of toxoid was given on the day of the wound, and tetanus developed on the eleventh day in spite of 1500 units of antitoxin finally given on the ninth day, in Case 8 a

dose of 1500 units of antitoxin was given, but not until the sixth day, and tetanus developed on the tenth day, in Case 9 only 750 units of antitoxin were given, — on the fifth day, — and tetanus developed on the eighth day, in Case 10 a dose of 1500 units of antitoxin was given on the second day, but was not repeated, and tetanus developed on the tenth day.

Failures to give proper specific prophylaxis to these patients were undoubtedly due to battlefield conditions. They nevertheless serve to illustrate the value of administering antitoxin to unimmunized personnel early, in proper amounts and with repeated doses.

Nine of the 10 patients had received considerable amounts of both penicillin and sulfadiazine for wound infection prior to the development of tetanus. One patient had received as much as 1,000,000 units of penicillin and 30 gm. of sulfadiazine, and another had received 400,000 units of penicillin and 40 gm. of sulfadiazine. These facts offer suggestive evidence that modern chemotherapeutic agents cannot be relied on — at least in the amounts mentioned — to prevent the development of the disease.

Type of Wound

Seven patients had compound fractures, 2 had penetrating flesh wounds, and 2 had severe burns. The following points need emphasis: the eschar of a contaminated burn creates ideal anaerobic conditions for the development of *Clostridium tetani*, and a small penetrating wound harboring pieces of dirt and clothing may prove more fertile soil for the organism than the larger and more dramatic wound that, in the normal course of events, attracts greater attention from the surgeon.

Diagnosis

The most important step in the diagnosis of tetanus is to think of it. Even after a case has occurred in a hospital and the staff has become alerted, the signs and symptoms are apt to be missed for twenty-four hours. Suspicion is often aroused by a nurse or ward attendant who calls the medical officer's attention to the fact that a patient is having difficulty in eating or in placing a thermometer into his mouth.

The speed with which tetanus develops from onset to clearcut symptomatology varies greatly from patient to patient. When the disease is fulminant, signs may be observed within a few hours of onset. Conversely, mild local tetanus may smolder along as local muscle spasm in the vicinity of a wound for several days before the appearance of spasm in other muscles makes the diagnosis unequivocal.

The so-called "lockjaw phenomenon" is usually the first overt sign and symptom of classic generalized tetanus. When a wounded man complains that he is having difficulty in opening his mouth,

proteins had been an important cause of death. As a result, studies of plasma protein, hemoglobin and hematocrit values were made, and in many cases these were found to be lowered. To such patients large amounts of plasma and whole blood were given intravenously in an effort to restore these values to normal. One patient received 5300 cc of blood and 500 cc. of plasma, and several others received 1500 to 2000 cc of blood.

Our observations led us to believe that these vigorous efforts to meet abnormally great nutritional demands were helpful both in supporting the patient through the critical stage of the disease and in shortening the period of convalescence.

Complications

Convulsions The prevention and treatment of convulsions involved nice judgment in the use of sedation, and it was soon found that the course to be followed was treacherous. On the one hand, too little sedation left the patient exposed to the dangers of severe spasms and convulsions. In one patient (Case 6) who was too lightly sedated spasm of the larynx with severe stridor relaxed only when the patient appeared on the point of death. Thereafter a tracheotomy set was kept in the treatment room. The last patient of the series (Case 10) appeared to be doing well on the seventh day when a sudden generalized convulsion occurred and the patient became extremely cyanotic and died in spite of all attempts at resuscitation, at autopsy, extensive atelectasis and intrapulmonary hemorrhages were found. On the other hand, it soon became obvious that too much sedation increased the danger of serious pulmonary complications. The patient with tetanus can scarcely expectorate through his clenched teeth and can take only shallow breaths, owing to the rigidity of the chest muscles. These factors alone render the patient easy prey to pulmonary atelectasis. When sedation is added in amounts sufficient to depress respiration and the cough reflex, the susceptibility to pulmonary complications is still further increased.

To avoid these two extremes, it was found advisable to give a regularly scheduled dose of sedative sufficient to blunt the edge of apprehension and keep the patient drowsy a good deal of the time without narcotizing him so deeply that he became difficult to arouse. Temporary increases in this basal dose were made whenever severe spasms threatened and before stimulating procedures, such as dressing the wound and replacing a stomach tube, were carried out. It proved imperative on several occasions also to have immediately available a parenteral sedative of the quick-action type.

Of the many sedatives suggested for use in the treatment of tetanus, we selected two and can report on them as being satisfactory. Paraldehyde met all the requisites: it could be given by mouth

or by rectum for prolonged basal sedation; it could be taken directly from the bottle into a syringe for intramuscular or intravenous injection to gain an immediate effect in an emergency, 4 to 6 cc of paraldehyde every three hours by mouth—or by means of a stomach tube—produced about the desired amount of basal sedation in most cases, and 2 to 4 cc intravenously or intramuscularly supplied rapid sedation successfully. The other sedative used was sodium amytal, which could be given by mouth in doses of 0.2 gm every three hours for basal sedation or by vein in doses of 0.3 gm for emergencies. After three or four days the patient's tolerance to these drugs usually showed a definite increase and the dosage was raised or a shift to the alternate sedative effected.

Since the aim is to give as little sedation as is consistent with protection from convulsive seizures, it is essential that the greatest advantage be taken of the sedation produced by the scheduled doses. Routine procedures involving handling of the patient should be so timed that they occur when the effect of the regularly scheduled dose is at its peak. By this means, extra doses may be avoided.

Infection To 8 patients, full doses of sulfadiazine (with equal amounts of sodium bicarbonate) were given by mouth, and 20,000 units of penicillin were given intramuscularly every three hours for three to seven days. These drugs were used for their bacteriostatic effect both on the tetanus bacillus and other pathogenic wound organisms and on pathogens in the respiratory tract to prevent pulmonary infection following atelectasis. In 2 patients (Cases 4 and 6) sulfadiazine was stopped because of a marked decrease in renal output. In one of these (Case 6) the drug was resumed with beneficial effect when pneumonia supervened.

Miscellaneous Since pulmonary atelectasis of minor or major degree was an almost universal complication, frequent turning of the patient in bed, voluntary coughing and intermittent inhalation of a mixture of 5 per cent carbon dioxide and 95 per cent oxygen were instituted as routine procedures for two or three days following operation. When atelectasis developed, care was taken that the affected lobe or lobes received frequent postural drainage. Several firm slaps on the back, with the patient turned on his face or lifted up by the hips, were helpful in some cases in loosening mucous plugs in the bronchial tree. Bronchoscopy and tracheal catheterization were not employed for fear that the local laryngeal irritation caused by these procedures might induce laryngeal spasm. Atelectasis, which was so widespread in 1 case that oxygen therapy by means of a B.L.B. mask was given for two days, in most cases proved an extremely troublesome and serious complication.

Two patients (Cases 7 and 10) suffered from retention of urine from spasm of the bladder sphincters. Inlying catheters were used for a few

so that several things are done at once and time is allowed for the patient to have uninterrupted rest for the succeeding interval. A three-hour schedule proved satisfactory in our hospital. The patient may be given sedation, penicillin, feeding, back massage, postural changes and intravenous therapy, if indicated, at intervals of three hours. After the first 3 cases, we learned that it was well worth while to have a mimeographed form on which there was space for every hour of the day and night for recording the therapy that was ordered and carried out. When these forms had been completed, they were filed chronologically in the attendant's room so that the medical officer could easily refer to them.

The main principles of treatment adopted were as follows: sufficient antitoxin was given to the patient to neutralize the effects of toxin that had been and was still being produced, so far as possible, the focus at which tetanus toxin was still being produced was removed, attempts were made to prevent and treat the complications of the disease, and general supportive treatment was given.

The administration of antitoxin involves a decision regarding the amount of antitoxin to be given and the route and speed of its administration. The factors affecting this decision are the length of the incubation period and the severity and rapidity of progression of the symptoms. Patients who had had a short incubation period and fulminating symptoms were considered to require large amounts of antitoxin, about one quarter of the total dose being given intravenously. In the slowly progressive form, in which mild symptoms developed over two or three days, we gave all antitoxin intramuscularly and in smaller amounts.

In the first 3 cases 70,000 to 80,000 (American) units of antitoxin was given—20,000 to 40,000 intravenously and the rest intramuscularly. The 3 patients died. These unfortunate results induced us to use between 120,000 and 180,000 units of antitoxin in the subsequent 7 cases, in this group, only 1 patient died. In 5 of these cases fulminating symptoms led us to give 20,000 to 40,000 units intravenously. The remainder was injected partly into the muscles in the vicinity of the wound and partly into the gluteal or thigh muscles. In all cases the great bulk of the antitoxin was administered as soon as possible after the diagnosis of tetanus had been made, usually during the operation for débridement of the wound. In 3 patients further progression of symptoms and a feeling of doubt concerning the elimination of the focus, such as widespread burns, induced us to give additional doses in the course of the ensuing week. Whenever antitoxin was administered, adrenalin in a syringe was available for immediate use.

The usual procedure was to perform a skin test for sensitivity to horse serum as soon as the diagnosis had been established. During the twenty minutes that were necessary for the observation of

the reaction to this test, the operating theater was alerted to make ready for débridement of the wound, and the previously selected personnel were summoned to prepare the rooms and equipment for the subsequent care of the patient. The allotted dose of antitoxin was administered during the operation.

Radical débridement of every wound was performed under intravenous Pentothal Sodium anesthesia. This is necessary, in our opinion, despite a history or evidence of previous débridement and despite the innocent appearance of slight wounds. Amputation, in 3 borderline cases, was considered justified, since the immediate threat to life from a residual focus of tetanus outweighed the handicap of a permanent deformity. In a patient with extensive burns it was considered necessary to employ widespread, meticulous surgical removal of necrotic tissue even despite the risk of some secondary hemorrhage. This was followed by activated zinc peroxide dressings, which were changed under anesthesia every two or three days until the areas remained clean. Postoperative wounds were usually dressed with penicillin compresses and in some cases with activated zinc peroxide.

When the patient was wheeled from the operating theater, two major steps in therapy had been accomplished: the focus of tetanus toxin production had been removed so far as was possible and the patient had received a large amount of antitoxin to offset the effects of toxin that had already been produced.

The caloric, protein, electrolyte and fluid requirements of the patient with tetanus are large because of high fever, constant muscle spasm, excessive sweating, infection, and loss of plasma and blood from the wound. To meet these demands, a stomach tube was introduced shortly after the patient's arrival from the operating room. By this route were subsequently given a daily diet of 3000 to 3500 calories containing 120 to 130 gm of protein and 3500 to 4000 cc of fluid. The tube proved an invaluable method of giving not only these nutrients but also medications such as sulfonamides, vitamins, sedatives and mineral oil. By the use of a tube of sufficient length, all these procedures could be effected without even waking the patient from sleep. It is difficult to get a tube in place in a patient with tetanus. We found it helpful to carry out this procedure shortly after a sedative had been given, when the patient's apprehension had been dulled and yet before the sedative had taken such effect that the patient was no longer co-operative. Once the tube was in place, our practice was to leave it there five or six days without renewal, since reinsertion often precipitated convulsive seizures. Evidence at autopsy, in an early and rapidly fatal case, of widespread tissue edema, in addition to pulmonary edema and pleural effusion, attracted our attention to the possibility that low plasma

proteins had been an important cause of death. As a result, studies of plasma protein, hemoglobin and hematocrit values were made, and in many cases these were found to be lowered. To such patients large amounts of plasma and whole blood were given intravenously in an effort to restore these values to normal. One patient received 5300 cc of blood and 500 cc. of plasma, and several others received 1500 to 2000 cc of blood.

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Two patients (Cases 7 and 10) suffered from retention of urine from spasm of the bladder sphincters. Inlying catheters were used for a few

days for relief of this symptom and to prevent constant changing of bed linen because of incontinence

Fecal impaction occurred in Case 4. The severe muscle spasms that were caused by its manual extraction induced us to give 30 cc of mineral oil, through the stomach tube, each night as a routine procedure to all subsequent patients. No other impactions developed.

SUMMARY

The experience in treating 10 cases of tetanus among German prisoners of war is reported. Of these 10 patients, 4 died.

The problems of tetanus prophylaxis are discussed and the necessity of adequate and repeated doses of prophylactic antitoxin in previously unimmunized personnel is stressed. The value of considering even slight wounds as possible foci of infection is pointed out, and some of the difficulties in diagnosis are discussed.

Attention is drawn to the difficulty of the therapeutic problem, and the management of these cases is described in detail, with emphasis on the importance of teamwork and constant individual attention for good therapeutic results.

PLASTIC SURGERY IN A MILITARY HOSPITAL*

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ORGANIZATION

The cases were divided into the following five general groups: maxillofacial, hand, orthopedic, eye, and general plastic.

Maxillofacial Section

These cases comprised all requiring the combined services of a plastic and a dental surgeon. The predominant type consisted of missile wounds of the mandible and maxilla, with a smaller percentage of fractured jaws due to vehicle injuries. There were also occasional cases of mandibular tumor and cyst, palatal defects and other abnormalities encountered in civilian life.

As soon as a history had been obtained and physical and x-ray examination had been completed, the patient was presented before a conference composed of a plastic surgeon, a dental surgeon and a liaison officer, the last being the ward officer directly in charge of all maxillofacial cases. At that time a program of treatment was outlined. In missile wounds of the jaws this usually consisted of the determination of the type of splint to be applied and a decision regarding the need for sequestrectomy. The patient was then followed in either the dental or the surgical department until the next phase of treatment, when he was again presented before the conference. At this stage the question of the need for a bone graft usually arose. When nonunion was evident the type of fixation and the kind of graft were determined. Iliac bone was used in most cases, although in cases of mild nonunion osteoperiosteal grafts sufficed. Rib grafts were occasionally employed to reconstruct fractures in the region of the angle or horizontal ramus.

The dental surgeon usually assisted at the operation and carried out postoperative oral care. Several weeks later the patient was again presented before

IN 1944 the Cushing General Hospital was designated as one of nine Army centers for plastic surgery operating within the continental limits of the United States. During the first twenty months a total of 1474 patients were admitted to this section, and two thousand one hundred and ninety-six operative procedures were carried out, with no operative or postoperative mortality.

The organization and functioning of this center is of interest, not only from the standpoint of its military pattern but also because of methods and procedures, developed in the face of reduced personnel, that might prove advantageous in the operation of any civilian hospital service. Also, military medicine has impressed on its participants the value of frequent consultation in the care of patients—a type of practice to which army medicine lends itself quite easily because of the concentration of patients, even with minor illnesses, in hospitals. This concept of directing the care of patients, which had previously been utilized to advantage at the Bushnell General Hospital, was expanded at this post to include the care of the majority of the plastic surgical cases.

The lack of trained personnel, as well as the frequent change, necessitated the most efficient utilization of the time of the two trained plastic surgeons and of those who had received special instruction. For this reason the cases were divided into several groups for the purpose of concentrating the care of patients in each of these categories and also for expediting the training of nurses and corpsmen by familiarizing them quickly with problems arising in the particular group under their jurisdiction.

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the conference to determine the stability of the graft and the need for further surgery prior to preparation of dentures. If the dentist considered the buccal or labial sulci inadequate, an epithelial inlay was scheduled, the dentist preparing a fixation splint for the stent prior to operation. Again, the dentist assisted at the operative procedure and carried out oral care during the convalescence, introducing a denture as soon as the grafts were stable.

Under this program the simultaneous care of the patient by two departments was closely integrated. With the plan for each patient outlined and recorded in the conference, loss of time was avoided and, of more importance, the operative procedures of both departments were correlated. Cases such as those with injudicious extraction of teeth needed for splint support in palatal repair or bone graft were reduced to a negligible number. During periods of change of personnel, the conference furnished a means of maintaining the continuity of treatment by both departments until new officers had acquired a grasp of the problems involved. It was the opinion of all concerned that the conference created a most harmonious environment that was mutually instructive and effectively eliminated the misunderstandings incident to a more remote type of collaboration.

Hand Section

A similar conference was set up for the administration of several hundred cases of hand injury. The predominant injury was the gunshot or shell-fragment wound, with a smaller group of burn scars and vehicle injuries.

The conference was directed by four persons, including plastic, neurosurgical and orthopedic surgeons and a physiotherapist. After initial study each case was presented before the conference, where a course of treatment was outlined and the patient sent to the appropriate ward. A majority of the patients with missile injuries were retained on the plastic wards because of a resurfacing problem. Occasionally, the defect could be covered by rotation of local tissues, but in most cases abdominal flaps—either tubed or direct—were utilized to cover the involved areas. In a few of the smaller defects around the web spaces, flaps from the opposite arm were employed. As soon as the resurfacing had been completed, the patient again appeared before the conference for review and was transferred either to the orthopedic service for tendon and bone work or in some cases to the neurosurgical service for nerve repair. It was often arranged in conference to have two services carry out a combined procedure, such as a nerve exploration or repair with a rotation or pedicle flap.

The patients with hand deformities resulting from burns were treated primarily on the plastic service, where resurfacing with free grafts was carried out as quickly as possible. These cases were also fol-

lowed in conference, where the counsel of the orthopedic surgeon in methods of splinting to minimize deformity was most valuable and where the presence of the physiotherapist integrated the surgical procedures with the graduated exercise that had to be started in the early postoperative course.

As time went on, each member of the conference became familiar with the usual methods of treatment proposed by the other members, and a number of modifications of therapy were carried out as a result of the integration of individual concepts of treatment. For example, the plastic surgeon's emphasis on the susceptibility of recent grafts to trauma led the physiotherapist to modify the treatment of this group of hand cases. All new technicians were carefully warned of the danger of too forceful massage, and the use of infrared lamps and whirlpool baths at the usual temperature was eliminated.

Orthopedic Section

This group of cases was composed mainly of missile wounds of the lower extremity, presenting some of the most trying problems in rehabilitation. The great majority of patients had been admitted on the orthopedic service, where the initial phase of treatment, consisting of the application of traction and casts and the exploration of draining wounds and sinuses, had been carried out. As soon as feasible many of these patients were brought to a conference composed of an orthopedic and a plastic surgeon, where the former surgeon presented his opinion of the type of bone and tendon reconstruction that would be needed in the future and the latter outlined a plan of resurfacing to permit the maximum surgery that might be anticipated.

Occasionally, free grafts were sufficient, but the average case required a much more stable integument, so that the usual recommendation for coverage was a direct pedicle flap transferred from the opposite leg or thigh. A few defects were in such a position or of such magnitude that the cross leg graft was not appropriate, and thoracoepigastric tubed pedicle flaps brought down via the wrist were necessary. Again, combined procedures were sometimes decided on. Rotation flaps to cover bony defects could be combined with iliac bone chips to fill depressed areas, either to increase stability of the affected bone or to fill cavities that could not be completely obliterated by the rotated flap. In multiple injuries two teams—an orthopedic and a plastic—arranged to carry out separate procedures on the same patient simultaneously.

Eye Section

Although comprising a smaller group than the ones mentioned above, the cases of missile wounds of the orbit presented rather complex problems for the integration of functions of the ophthalmologist, neurosurgeon, plastic surgeon and the ocular pros-

thetic department. Many of these patients had suffered loss of a portion of the bony wall of the orbit, with or without involvement of the dura. Patients in whom the only problem was restoration of bony contour of the supraorbital or latero-orbital region were treated on the neurosurgical service, usually by the introduction of a moulded tantalum or lucite plate. When there was associated deformity of the soft tissues of the orbit, it was usual to carry out reconstruction of the lids and conjunctival sacs before the tantalum plate was introduced.

The intraorbital reconstruction was planned in conjunction with the ophthalmologist and the dental surgeon in charge of the construction of acrylic prostheses. In general, the first problem was replacement or reconstruction of the lids. Adjacent flaps or free grafts were used in almost every case, to afford external covering, with the introduction of ear cartilage when necessary to provide support. The adequacy of the conjunctival sac was then evaluated. Occasionally, in questionable cases, the prosthetist was able to dilate a sac of borderline dimensions with graduated conformers and to obviate the need for grafting. In the severer injuries mucous-membrane grafts were introduced to enlarge the socket, and as soon as the graft was healed, the patient was transferred to the prosthetic department, where a conformer was inserted immediately to prevent contracture of the graft. While the final prosthesis was being constructed, minor revisions such as eyelash grafts were carried out.

General Plastic Section

In all cases that did not fall into the special categories listed above the patients were admitted to a general plastic section, where there was no significant duplication with other surgical fields.

Many cases of severe facial burn presented problems in the reconstruction of deformed ears, partial nasal loss, lip contractures and loss of cheek, forehead and orbital skin. Ear reconstruction was performed by the use of adjacent retroauricular skin when the loss was confined to the helix, in more extensive losses, it was necessary to restore cartilage support by means of preserved rib cartilage taken during autopsies and kept under sterile conditions until needed. If the retroauricular skin had been severely damaged by the original trauma, the scar was replaced by a free skin graft, which was later used for the auricular reconstruction.

Preserved cartilage was also used extensively for building up depressions of the infraorbital ridge and malar region. These fractures were well consolidated by the time of arrival at the hospital, so that no attempt at repositioning was made, even in cases in which no loss of substance had occurred. Cartilage was used both in the form of carved blocks and in the form of diced material, and occasionally in combinations of the two.

Nasal deformities varied from relatively minor losses from burns to total nasal loss due to shell fragments. The small losses of the alar rim were restored by free grafts from the rim of the ear, including a strip of cartilage for support. The more extensive losses required either pedicle flaps from the forehead or tubed flaps from the cervical or humeral regions.

Deformities about the mouth at times presented complex problems in reconstruction. Whenever possible the reconstruction was performed by rotating skin from the adjacent cheek or cervical region to afford a covering that most closely matched in color* and texture the absent tissues. Occasionally the defect was too extensive for such procedures and tubed pedicle flaps from the lower neck, acromipectoral region or thoracoepigastric region were utilized.

Operating and Dressing Rooms

To utilize to the maximum degree the available time of the trained members of the staff, it was frequently possible to have two teams supervised by one plastic surgeon. This was not considered in any sense an ideal situation but offered a practical expedient to aid in keeping up with the required work. Furthermore, it was considered essential to eliminate so far as possible all delay between operative cases.

The preparation of a plastic case for operation often requires a good deal of time—for example, when, to resurface a hand, the affected hand and forearm and the donor area, such as the abdomen, chest or thigh, must be prepared. To eliminate the delay of preparing a patient in the operating room, the following routine was established. After a period of instruction, a nurse selected as the supervisor of preoperative preparation was able to acquire a firm grasp of the principles involved in the preparation of plastic patients. Corpsmen were assigned to function under her jurisdiction. Patients arriving at the operating pavilion were taken to a preparation room where a detailed description of the field of operation, submitted by the surgeon on the operative slip, was available. All operative fields were shaved, thoroughly cleansed with soap, alcohol, ether and Zephiran and covered with sterile towels, the patient being retained in the preparation room until an operating room was free, when he was transferred to an operating table and the draping was completed. In the preparation of facial cases, pontocaine drops were administered to the eyes to prevent discomfort. In this way it was possible to

*Facilities eventually became available for the artificial pigmentation of scars and grafts conspicuous because of color tones that contrasted sharply with the surrounding tissues. The success of this technique which was essentially the tattooing of the unsightly area with blended mineral pigments depended in large part on the appreciation of color tones and on the ability of the operator to keep the shading on the light side rather than creating an overly dark tone, which was much more difficult to correct. This part of the program was delegated to an artist associated with the department whose previous training in the blending of colors gave him particular qualification in this field.

complete almost all types of preparation before the anesthetic was administered, from ten to forty minutes' delay in the operating room being thus avoided

Another feature that not only saved considerable time but also prevented confusion and omissions in postoperative care was the organization of the dressing section. Two large and completely equipped dressing rooms, as well as two smaller supplementary dressing rooms, were put in operation as soon as possible, and in the great majority of cases post-operative treatment was carried out in these centralized spots. A nurse was placed in charge of the entire dressing section and given the responsibility of training newly assigned nurses in plastic procedures. The dressing nurses worked on a full-time basis in the dressing rooms and did not have ward responsibilities. When the program was well under way, about nine hundred dressings, or 85 per cent of the total number, were carried out weekly by nurses without supervision.

Toward the end of each operation, the operator dictated two sets of instructions, the usual post-operative orders and, on a separate sheet, the dressing orders. Each dressing-order sheet was sent directly to the proper dressing room, where dates of dressings were filed and a list of his own dressings sent daily to each surgeon, delays and omissions in aftercare being thereby eliminated.

SUMMARY

In organizing the plastic surgery section of an Army hospital in the United States, it was found expedient to divide patients into five categories for purposes of administration and professional care. A conference system was established to integrate plastic surgical procedures, with necessary and concomitant treatment by other services, the method of operating these conferences is described. Several practical points in expediting operative and post-operative treatment are discussed.

MEDICAL PROGRESS

PHYSIOLOGY (Concluded)*

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TOXIC AND HEPATIC FACTORS IN SHOCK

It is now generally agreed that the primary factor in the development of the shock syndrome is a reduction in the effective volume of circulating blood. Whether through hemorrhage, vasodilatation in traumatized regions of the body or loss of fluid through damaged blood vessels in those areas, a discrepancy between the capacity of the vascular system and the amount of blood available to fill it occurs, and the blood pressure falls. If this discrepancy is too great, the body's compensatory mechanisms are overwhelmed, and death quickly follows. With a somewhat lesser degree of oligemia this does not happen, but the blood pressure is more or less rapidly brought back to normal, and spontaneous recovery takes place. In dogs this may occur after bleeding of as much as 30 to 40 per cent of blood volume.³⁹ Somewhere between these two extremes, there appears the condition known as shock in which compensation is adequate only to maintain a prolonged period of hypotension at the end of which the victim finally succumbs. During the greater part of the hypotensive period the condition is reversible, and if adequate replacement therapy is carried out, the animal re-

covers. In the terminal stages, however, the condition becomes irreversible, and despite transfusion or other treatment, recovery does not occur. Much of the recent work on the shock problem has centered around the question of the factors involved in the transition from the reversible to the irreversible stage.

It is clear that continuation of hemorrhage or the further loss of fluid through damaged capillaries in the traumatized region can be and probably is often responsible for the terminal failure of compensation. These factors cannot, however, be the only or even the major ones that operate at this point. Thus, Scott⁴⁰ compared the increase of leg volume in tourniquet shock in dogs and showed that no difference can be demonstrated between the dogs that die and those that recover. The leg volume of dogs that recovered increased on an average by 3.69 per cent of the body weight, whereas in a comparable series of animals dying from early shock the total volume increase was 3.43 per cent of body weight and in a group of animals in deeper shock fatal to all animals, the volume increase was 4.03 per cent of body weight. Friedberg and Katz⁴¹ applied plaster casts to the legs of dogs shocked by venous occlusion in an attempt to prevent local fluid loss, but were unable to reduce the mortality of the procedure in this way.

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Haist and Hamilton⁶² found that by reclamping the legs of animals shocked by the tourniquet method before the stage of irreversibility had set in, it was possible to produce recovery despite the fact that all or nearly all the fluid loss into the traumatized leg had already occurred. Green and co-workers⁶³ found that fatal shock could be produced by the tourniquet method in fully anesthetized dogs with a fluid loss of an average of 18 cc per kilogram — appreciably less than the fatal hemorrhage volume, which amounts to 50 cc per kilogram or more. These workers concluded that although the initial fall of arterial pressure of dogs traumatized by this procedure is induced principally by a combination of reactive vasodilatation in the traumatized legs and initial rapid loss of body fluid into the traumatized tissues, the continuing steady decline of arterial pressure is probably due to a continuing smaller loss of fluid into the traumatized tissues, as well as to the onset of a vicious circle whereby the reduced systemic blood flow results in widespread damage to the vascular system and perhaps also to other tissues.⁶⁴

An attractive concept of the vascular changes by which this vicious circle is introduced is afforded by the recent studies of Chambers and his associates,⁶⁵⁻⁶⁸ who studied, in the mesenteries of various animals, the response of the small blood vessels to hemorrhage and trauma. Following hemorrhage or trauma there is a marked increase in the activity of the small arterioles and metarterioles characterized by marked vasoconstriction of the vessels and increase in the rate of their rhythmic dilatations and constriction that these authors call vasomotion, as well as such an increase in the sensitivity to adrenalin that complete local shutdowns of circulation may take place on injection of a 1:60,000,000 solution of adrenalin. Because of precapillary constriction, capillary flow is restricted to central channels. Flow through the open capillaries is nevertheless rapid and unidirectional. During the next reversible stage of low blood pressure, vasomotion diminishes and the contractile phase becomes progressively shorter. The response to adrenalin falls toward normal. There is a marked slowing of the flow in the capillaries and an increase in the number of capillaries having a blood flow because of the diminished vasomotion. Venules begin to dilate, and the venous flow is sluggish. Finally the hyporeactive stage is reached in which vasomotion ceases in dilatation. The response to adrenalin is greatly reduced, only a fleeting response occurring to the injection of a 1:2,000,000 solution of adrenalin. The arterioles begin to dilate, stagnation of blood occurs in the many open capillaries and venules and venular capillaries become distended by back flow. When this stage is reached, further transfusion is without effect and the transfused blood is trapped along with much of the other blood in widely dilated stagnant capillaries. According to these authors, therefore, the essential factor in the change to the irreversible stage is the loss of tone and the

development of irresponsiveness in the small peripheral blood vessels that so reduces the effective circulating blood volume that the blood pressure can no longer be maintained. Fine and Seligman⁶⁹ came to much the same conclusion from the study of the distribution of radioactive proteins introduced into the blood stream in hemorrhagic shock.

In explaining the mechanism of these changes in small peripheral vessels, which appear to lie at the root of the problem, a good case can be made out for the action of local tissue anoxia. It is clear from the work of Chambers and his co-workers that blood flow in the viscera must be markedly reduced in all stages of shock and that this is apparently even more pronounced in the peripheral system. Thus, Levinson and Essex,⁷⁰ among others, have studied the response of the ear vessels of rabbits through transparent chambers inserted in the ears of animals in traumatic shock. They noted that, as the period of onset of shock approached, there were phases when the blood flow in the chamber was shut off through arteriolar constriction. The effect of such vasoconstriction is, of course, to reduce markedly the blood flow in many organs of the body. Dole et al.⁷¹ estimated renal blood flow in dogs by means of para-aminohippuric acid and creatinine excretion rates and found the blood flow ranging from 4.6 to 12.0 liters per minute per kilogram of kidney in normal animals before hemorrhage, after hemorrhage the blood flow ranged from 0 to 3.84 liters per minute per kilogram. The latter figure was obtained in an animal having a blood flow of 6.72 liters at a blood pressure of 138 mm of mercury, and the value of 3.84 liters was obtained on reduction of the blood pressure by hemorrhage to 120 mm. In consequence, there is a greater extraction of oxygen from what blood does flow through most organs of the body, and venous blood returns to the heart with much less than its normal content of blood.⁷²

From the work of Shorr, Zweifach and Furchgott,⁷³ however, it appears that the depression of peripheral blood vessels is produced by the action of a humoral substance referred to by them as VDM (vasodepressor material), which is elaborated by skeletal muscles and by the liver. The material is apparently formed by muscles in small quantities in the compensatory stages of shock, but not by the liver at this time, nor does it appear in the blood stream of animals in the preirreversible stages, when the liver is capable of destroying or inactivating the material. With the onset of irreversibility, the liver not only fails to protect the circulation against the larger quantities of VDM that escape from skeletal muscles but also contributes significant quantities of the material itself. The cause of this change in liver function is the failure of the oxygen supply to that organ.

The liver is unique among the organs of the body in receiving the larger part of its oxygen supply from the venous system. McMichael⁷⁴ found that in the

cat about two thirds of the oxygen supply of the liver comes from the portal vein under normal conditions of blood pressure. The oxygen content of the hepatic vein is always less than that of the portal vein, and obstruction of the portal vein to a lobe causes central degeneration in its lobules. Naturally, then, the liver is especially vulnerable to the great reduction in the oxygen content of venous blood that occurs in the compensation state of shock, and in the experiments of McMichael the average saturation of portal venous blood fell from 50 per cent when the mean arterial pressure was 180 mm of mercury to only 25 per cent when, because of hemorrhage, the mean arterial blood pressure fell to 90 mm. It is now known that this deficiency of oxygen causes a number of changes in liver function. The liver loses its ability to store glycogen,⁶² and the rate of replacement of plasma protein after hemorrhage is diminished.^{75, 76} Thus, a normal unanesthetized dog not in shock replaces from 10 to 29 per cent of its total prehemorrhage plasma proteins within twelve hours after the hemorrhage, or a total weight of from 6 to 15 gm, whereas dogs in shock replace only about a tenth of this amount in the same time. Amino acids increase in concentration in the blood owing to an increased production due to protein breakdown in peripheral tissue, either because of direct trauma or because of anoxia and because the damaged liver can no longer readily deaminate them.^{77, 78} Disturbance of carbohydrate metabolism can be seen in the increase in the level of lactic and pyruvic acid in the blood,⁷⁹ and the oxygen consumption of liver slices falls off. Whereas liver slices from normal animals consume an average of 5.6 cu. mm for each milligram of initial dry weight of tissue per hour, the liver from animals in a fair state after hemorrhage consumes but 3.6 cu. mm and that from animals in a poor state only 1.82 cu. mm. It should be noted that in rats, especially those recently fed, the effects of shock on the liver are not so marked as those in fasted rats, and in fact in fed rats the liver is also apparently more resistant to anoxia.⁸⁰ The liver also loses approximately 10 to 25 per cent of its total potassium content during the course of shock or anoxia.⁸¹

As might be expected, the inhalation of pure oxygen in hemorrhagic shock is not of great assistance in improving the situation so far as the liver is concerned, inasmuch as the arterial blood saturation does not fall markedly during the critical preshock stage and the anoxia of the liver depends rather on the increased extraction of oxygen in the face of a diminished blood flow. Wood, Mason and Blalock,⁸² however, report experiments in hemorrhagic shock in dogs in which inhalation of pure oxygen increased the content of portal venous blood from 12.52 to 15.21 vol per cent. Frank, Seligman and Fine⁸³ shocked dogs by hemorrhage and continued low blood pressures for approximately two to four hours. Animals that were then perfused by exchange circulation with donor animals in which arterial blood

from the donor entered the jugular vein were not helped by the procedure, and nearly all died. On the other hand, cross circulation in the same way, except that the arterial blood of the donor entered the shocked animal through the splenic vein and therefore added arterial blood to the portal circulation, made it possible for 11 of 12 animals thus treated to survive. It is obvious that preservation of liver function is of crucial importance in recovery from advanced hemorrhagic and other types of shock and that the essential factor is the maintenance of an adequate oxygen supply to the liver.

Apart from the apparently physiologic V.D.M., bacterial toxin must also be considered, at least in experimental shock. Aub and co-workers⁸⁴ found toxin due to the presence of a *Clostridium* exotoxin in 28 per cent of experiments in which fluid was collected from traumatized muscles and injected into normal dogs. Prinzmetal, Freed and Kruger⁸⁵ found that shock was produced in 9 of 12 dogs when the quadriceps muscle was removed with aseptic precaution, crushed and replaced. When the muscle was removed and replaced without crushing, shock was not produced. If bacterial growth was prevented by appropriate bacteriostatic agents, shock did not occur. It is also apparent that damaged muscles lose potassium in large quantities and that in appropriate circumstances, more particularly when kidney function is suppressed, this ion may have a toxic effect.⁸⁶⁻⁹⁰ Bacterial toxin, but not potassium, might account for the shock reported in normal animals that are cross-perfused with animals in shock from application of tourniquets.⁹¹ In hemorrhagic shock Frank, Seligman and Fine⁸³ failed to find signs of shock in the normal animal used for cross circulation with a shocked animal.

From all this material it is possible to put forward the following view of the events that transpire in the course of hemorrhagic or traumatic shock. A reduction in effective blood volume through hemorrhage or through vasodilatation and loss of plasma in damaged regions occurs. Compensation for the diminished blood volume takes place by means of increased arterial or venous constriction, — at least in part on a sympathetic basis,⁹² — and an increased vasomotor activity in the metarterioles and precapillaries is due to the production of a vasoexcitator substance from the kidney⁷³ that may be the same as the renal hypertensive material liberated as the result of renal ischemia — it is known that the kidney removes only a small proportion of the oxygen from the blood that circulates through it, and even when blood flow is markedly reduced, it is not able to increase its utilization.^{71, 93} There is also some evidence that the vasoconstrictor substances are produced in shock even in the absence of the kidneys.⁹⁴ If, as a result of these compensatory measures, peripheral blood flow is excessively curtailed, the oxygen content of the portal venous blood becomes dangerously low, and the liver begins to suffer from

anoxia. It therefore fails to destroy the relatively small quantities of VDM produced by the damaged or partially anoxic tissues and, in addition, produces VDM itself. This material, which acts on the peripheral vessels to cause vasodilatation and stagnation of blood in an increased number of open capillaries, thus further reduces effective blood volume and sets up a vicious circle of lowered blood pressure, further tissue and hepatic anoxia and, as a consequence, further release of VDM.

THE ARTIFICIAL KIDNEY

The results of animal experimentation have for some time held out the promise that uremia and anuria in man might be treated by the removal of the abnormal accumulation of metabolic products by their dialysis through the membranes of artificial kidneys or through natural membranes, such as the peritoneum⁹⁵⁻⁹⁸. These attempts stem directly or indirectly from the work of Abel and his associates⁹⁹⁻¹⁰¹ in the years preceding World War I. The general concept of finding some substitute for impaired renal function is, of course, of much earlier origin. Thus, Abel recognized his predecessors in the method, to which he gave the name plasmapheresis, in which blood was drawn from nephrectomized animals, centrifuged and separated from the plasma and the washed corpuscles returned to the animal in Locke's solution. Other less direct methods have also been suggested, as well as the method of cross circulation with an animal with normal kidneys proposed by Nyiri¹⁰² from consideration of the fact that in parabiotic animals — that is, surgically created Siamese twins in which vascular intercommunication has been established across the communicating bridge of tissue — a single kidney may be sufficient for the excretory processes of both animals. Nyiri performed two successful experiments in one the donor dog was nephrectomized and in the other the dog was rendered uremic by uranium poisoning. In both the nonprotein nitrogen of the donor dog fell, whereas that of the recipient rose, only to be excreted without damage to the normal animal. Other experiments failed, however, because of clotting in the communicating tubes. With the introduction of more active preparations of heparin this difficulty was overcome, and Thalheimer^{103,104} was able to simplify the technical problems by the method of exchange transfusions. By this method approximately 200 cc of blood was exchanged between an anuric and a normal dog and the process repeated twenty to forty times. Thus, in one experiment, the nonprotein nitrogen of the anuric animal fell from 75 to 61 mg per 100 cc after twenty exchanges and to 54 mg after forty. At the same time, the nonprotein nitrogen concentration of the normal dog rose from 22.5 to 36.5 mg per 100 cc, but this was excreted in a short time without harming the animal.

The method of Abel, Rowntree and Turner,⁹⁹ however, envisaged the utilization of an artificial mem-

brane constructed of collodion tubes through which arterial blood flowed only to return to the animal through an appropriate vein. The dialyzing tubes were then immersed in a fluid bath, in which substances might diffuse from the blood, and the diffusion of the substances out of the blood could then be regulated by variation in the composition of this fluid. If the fluid was of the same composition as normal plasma, the apparatus could be expected to remove only abnormal constituents or normal constituents present in abnormal concentration. The authors made the following observations:

Any constituent of the blood which it is desired to retain in the animal's system may be prevented from dialyzing out by the addition of the proper amount to the outer fluid. Where the object of the experiment is merely to remove from the blood abnormal constituents, as e.g., poisons, or constituents specifically secreted into the blood by a certain organ, normal serum from a similar animal may be used, thus insuring complete balance of all normal constituents, inside and out.

Hirudin prepared from the heads of leeches was used as an anticoagulant. There was a considerable fall in blood pressure when the apparatus was put into operation when a dog weighing 5.8 kg was connected to a dialyzer consisting of sixteen tubes each 20 cm long and 8 mm in diameter, the apparatus containing in all 200 cc, the arterial blood pressure (presumably, the mean pressure) fell from 120 mm of mercury to 64 mm. Lung edema was noted in some experiments. The method was used to collect various normal and abnormal material from the blood, and it was shown that nonprotein nitrogen constituents appeared in the dialysate in approximately the proportions in which they existed in the blood. It was, however, apparently Necheles^{105,106} who first used the method to reduce the nonprotein nitrogen of nephrectomized dogs. In two experiments the nonprotein nitrogen was reduced from 122 to 101 and from 218 to 161 mg per 100 cc, respectively, by several hours' diffusion through a dialyzing apparatus constructed of ten tubes of gold-beater skin having a total area of approximately 4000 sq cm. Apparently, Haas^{107,108} also had success in the dialysis of blood in living dogs with a collodion-tube apparatus patterned after Abel's, but had difficulty owing to the toxicity of the hirudin he employed. When he was able to obtain less toxic preparations of this anticoagulant, further experiments on dogs were carried out and a single short experiment was tried in man, a relatively short tube system being used. In the fifteen minutes of the experiment an indican clearance of 150 cc was established.

The successful application of this technic in man was made possible by the development of heparin and of cellophane from which a dialyzing tube 23 mm wide and about 45 meters long was constructed by Kolff and Berk^{96,98}. Through this tube blood was transported in small quantities at a time to ensure spreading over a large surface and thus increas-

ing the rate of dialysis. Blood was dialyzed against a solution containing 0.6 per cent sodium chloride, 0.2 per cent sodium bicarbonate, 0.04 per cent potassium chloride and 0.5 to 2.0 per cent glucose. In the absence of calcium from the dialyzing solution this ion was lost from the blood and was replaced by intravenous injection of calcium gluconate. In trials of the apparatus in patients suffering from anuria it was possible to remove large quantities of nonprotein nitrogenous material from the blood, and it appears that in the second case, as reported by Snapper,⁹⁵ the life of the patient was in fact saved. On the eighth day of anuria the blood urea nitrogen was 184 mg and the serum potassium 55 mg per 100 cc, the patient was comatose, and there was edema of the buttocks and legs. Dialysis through the artificial kidney was carried out for eleven and a half hours, during which 80 liters of blood was circulated through the apparatus and 60 gm of urea removed. The blood urea nitrogen fell to 57 mg and the serum potassium to 19 mg per 100 cc. It is apparent that at a serum potassium level of 55 mg per 100 cc the lethal limits had practically been reached and death was to be expected at any time. Death from this cause being averted by the removal of the excess potassium, the patient's life was preserved for another day, and by that time renal function had begun to reappear and the patient recovered.

Impressed by the difficulties with clotting encountered by workers in the preheparin days, Ganter¹⁰⁹ employed the peritoneum itself as a dialyzing membrane, he reported a case of uremia with pleural effusion in which replacement of 750 cc of pleural fluid by saline was followed by clinical improvement. He also successfully reduced the nonprotein nitrogen of anuric guinea pigs and rabbits by intraperitoneal lavage with saline. Rosenak and Siwon¹¹⁰ then suggested a constant intraperitoneal perfusion at the rate of 1 to 4 liters per hour, believing that the rate of diffusion of materials into the perfusing solution would be more rapid if it were constantly refreshed with new fluid. Since that time practically all workers have employed the constant-drip method, although it is clear from the work of Darrow and his associates¹¹¹ that fluid left in the peritoneal cavity rapidly comes into equilibrium with blood and that the nonprotein nitrogen content of this fluid equals that of blood within fifteen to twenty minutes. Although it was apparent from these and other investigations¹¹²⁻¹¹⁴ that the method might temporarily reduce the nonprotein nitrogen and diminish the symptoms of uremia, there was little evidence that the life of the uremic animal could thereby be prolonged, and it is apparent that infection posed a considerable problem. The method was nevertheless employed in man by Balázs and Rosenak,¹¹⁵ who perfused the peritoneal cavity of 2 patients suffering from uremia consequent to mercury poisoning with 12 liters of fluid. In the first case, in which the patient was

perfused for half an hour with a 4.2 per cent dextrose solution, the nonprotein nitrogen fell from 184 to 158 mg per 100 cc, whereas in the second case, after perfusion for an hour and a half with 19 liters of an 0.8 per cent sodium chloride solution, the nonprotein nitrogen fell from 149 to 139 mg per 100 cc. By the introduction of a rigid aseptic technic assisted by the use of penicillin and sulfadiazine, Seligman, Frank and Fine¹¹⁶ were able to prolong the period of dialysis to permit nearly continuous irrigation for twenty-four to thirty-six hours at a full rate of 25 to 35 cc per minute and thereby to control uremic symptoms effectively and to produce marked reduction in blood urea concentration in dogs rendered anuric by bilateral nephrectomy. Once the nonprotein nitrogen was lowered to more normal concentrations, shorter periods of dialysis (from eight to ten hours) carried out once in every twenty-four hours proved sufficient to maintain the animal, and it is clear that life in these animals was prolonged for from three to ten days. Abbott and Shea¹¹⁷ report an animal kept alive for nine days after bilateral nephrectomy, which also represents a clear prolongation of the survival period. Finally, the Boston workers have reported the successful treatment of uremia following sulfadiazine therapy in which the therapy was begun after eight days of almost complete anuria. After four days of perfusion, the blood urea concentration fell from 72.7 to 37.8 mg per 100 cc. Clinical improvement was noted, and on the fourth day urine flow began again. The daily urea output by peritoneal drainage varied from 12 to 20 gm per day, and the blood urea clearance averaged nearly 15 cc of blood per minute. Despite extreme care and the liberal use of penicillin, signs of peritoneal infection appeared but did not interfere with the successful treatment of the patient.

TREATMENT OF DEHYDRATION IN INFANTS

In a previous report in this series,⁸⁶ attention was called to the fact that in cases of water deprivation or loss of body fluid there is an extra secretion of potassium unassociated with nitrogen loss in the urine. By the excretion of such potassium in a higher concentration in urine than it was found in cell water, the body was able to retain cell water in the plasma and thus to mitigate the loss of extracellular fluid. The pediatricians were among the first to note this phenomenon, which was reported by Gamble and co-workers¹¹⁸⁻¹¹⁹ in fasting diabetic children and in diarrheal disease in children. Darrow¹²⁰ has recently estimated the amount of intracellular potassium lost in cases of severe dehydration due to diarrhea in infants and has found cases in which the total loss of intracellular potassium amounted to approximately one fourth of the estimated normal potassium content of the body.

It is known that a deficiency of potassium is not without harmful effects, the paralysis of familial periodic paralysis is one such condition, and muscular

weakness may be produced in man and experimental animals when potassium is excessively low. More important, a low potassium level is associated with the development of heart failure, with recovery when adequate potassium is administered, and both muscular and myocardial weakness have been noted in infants suffering from the dehydration of diarrhea. These facts and the general consideration that replacement therapy ought on theoretical grounds to be complete have led Govan and Darrow¹²¹ to use potassium in the treatment of the dehydration of diarrhea in infants. After the initial treatment of shock, replacement of fluid was effected during the first twenty-four hours by parenteral administration of from 80 to 150 cc per kilogram of body weight of a mixture of potassium chloride, sodium chloride and sodium lactate. After the first day smaller amounts (20 to 50 cc per kilogram of body weight) were given daily so long as the stools remained watery. In some cases from 1 to 2 gm of potassium chloride was added to each day's feeding when oral feeding was begun. The new method of treatment was instituted in September, during the preceding two months 53 patients had been treated by the conventional method, and 17 had died. During September and October, 50 patients were treated by the new method, and only 3 died. In general, the potassium therapy did not shorten the period of diarrhea, but it did enable the infants to withstand a disease that would otherwise have been fatal.

The most significant complication of the treatment may prove to be potassium intoxication. Many patients are presented in a state of shock after a considerable period of illness. In such circumstances the combination of tissue anoxia and low renal output may lead to the development of deceptively high concentrations of potassium within the serum. The immediate administration of potassium-enriched fluids to such patients may be dangerous, as was shown in the case of potassium intoxication reported by Govan and Weiseth¹²² in which a serum potassium level of 12.3 milliequiv per liter was noted and the typical, premortal, intraventricular block developed. Fortunately, the condition was recognized, and recovery was complete after the administration of 15 cc of calcium gluconate and 150 cc of hypertonic glucose solution. It has therefore been suggested that in the period of shock in moribund patients and perhaps in all cases of severe diarrhea, infusions of physiologic saline and glucose solution should be initiated for an hour or until urine formation is assured, after which the solution containing potassium chloride can be started. So characteristic are the electrocardiographic signs of potassium intoxication that this instrument, in combination with a cardioscope, or one of the modern visual writing instruments, might well be employed as a constant check on the rate and quantity of potassium infusion.

SPLenic HORMONE CONTROL OF PLATELET FORMATION

Although it seems well established from the work of Taylor and others described in an earlier report in this series¹²³ that platelets play no great part in the primary mechanisms responsible for blood clotting, it is equally obvious that they are important in causing clot retraction and in sealing off injured capillaries after damage. Whatever their specific function may be, bleeding takes place when they are excessively reduced in the blood stream, and a dramatic increase in the number of platelets occurs along with cessation of symptoms when the spleen is removed. A paper by Dameshek and Miller¹²⁴ provides the major outline of an acceptable theory of platelet regulation. Studying the megakaryocytes of sternal bone-marrow punctures in 10 patients with normal hematologic findings, they established a normal megakaryocyte count of not more than 300 per million nucleated cells. About two thirds of these megakaryocytes contained platelets or platelet-like bodies at the periphery of the cytoplasm and were apparently actively producing platelets. Differential counts of megakaryocytes were made in 5 cases of acute idiopathic thrombocytopenic purpura before splenectomy, and it was found that the number of megakaryocytes per million nucleated blood cells was on the average three times greater than that in normal subjects and only about 14 per cent of the megakaryocytes showed obvious platelet production. Following splenectomy, the number of platelets became sharply increased and approximately 73 per cent of megakaryocytes showed platelet production. Huge masses of platelets were seen extruding from previously unproductive megakaryocytes, and these also occupied large parts of the microscopic field.

The hormonal nature of the influence exerted by the spleen on platelet production was suggested as early as 1915 by Frank, who with Mines, in 1917, held the belief that the material was a toxic substance.¹²⁴ In 1938 Troland and Lee¹²⁵ described the extraction, from the spleens of patients suffering from idiopathic thrombocytopenic purpura, of a material that reduced the number of platelets in the circulating blood of rabbits, cats, dogs and monkeys when injected in fairly large amounts. Since that time the observation has been confirmed by a number of other investigators, but not by all.¹²⁶⁻¹³¹ The concept held by Dameshek and Miller¹²⁴ regarding the pathogenesis of the disease is that it is due fundamentally to an abnormality of the spleen that exerts an unusual effect on the production of platelets from megakaryocytes in the bone marrow by arresting the maturation of megakaryocytes. They postulate a hormonal relation between the spleen and the bone marrow and describe the condition as hypersplenism or hypersplenic thrombocytopenia.

This implies that the spleen normally regulates the maturation of megakaryocytes by the release of smaller quantities of its hormone, and Dameshek and Miller point to the persistently high platelet level that may be present for long periods after removal of a normal spleen. They also point to the association of thrombocytopenia with other conditions in which splenomegaly occurs. Although Dameshek and Miller have confirmed the presence of a platelet-reducing substance in extracts of spleens from cases of idiopathic thrombocytopenic purpura, the final link in the chain of evidence requires to be forged — namely, the unequivocal demonstration that an extract of normal spleen can cause a fall in platelet count. The hormonal studies also need to be controlled by means of bone-marrow punctures to demonstrate that the reduction of thrombocytes following injection of extract results from the arrest of megakaryocytic delivery of thrombocytes and not from nonspecific toxic action on the platelets themselves. Some observers have noted that, following reduction of thrombocytes by injection of extracts, there is occasionally a temporary thrombocytosis in the recovery phase. This suggests that failure of platelet delivery is in fact involved and that once the barriers to delivery are removed, the platelets again flood into the blood stream.

PITUITARY-ADRENAL HORMONAL CONTROL OF LYMPHOCYTES

The nature of the hormonal regulation of another formed element of the blood, the lymphocyte, together with the physiologic significance of the reaction, has recently been elucidated through the work of White and Dougherty,¹³²⁻¹³⁶ reviewed recently by Cope and Rosenfeld.¹³⁷ According to these investigators the influence of the adrenal cortex on lymphoid tissue was first noted by Addison, who observed hyperplasia of this tissue in the disease that bears his name. Lymphoid-tissue hyperplasia is also found in experimental animals after adrenalectomy, whereas adrenocortical hypertrophy and injection of adrenocortical hormone cause involution of the thymus and other lymphoid tissue. These adrenocortical effects are in turn under control by the pituitary gland, for injection of pituitary adrenotropic hormone produces a profound lymphopenia that does not appear if the pituitary hormone is given to adrenalectomized animals. Only compounds of the adrenal cortex that have a gluconeogenic function (compound E of Kendall) induce lymphopenia, which results from the failure of delivery of lymphocytes into the circulation because of profound degenerative changes taking place in lymphoid tissue. These changes were found within an hour after the injection of either adrenotropic or adrenocortical hormone and persisted for as long as six hours. They were characterized by pyknosis of medium-size and small lymphocytes, the shedding of the cytoplasm of lymphocytes, a decreased number

of lymphocytes in the lymphoid tissue and extreme edema of all lymphatic structures studied. During this period mitosis ceased. Concomitantly, there was an increase in the serum protein associated with the gamma globulin fraction and an increase in circulating antibodies. From this time relation among histologic changes in lymphoid tissue, blood lymphocyte levels, serum protein concentrations and antibody titers, the authors concluded that a portion of the increased serum protein is antibody globulin derived from lymphocyte dissolution. This mechanism is shown by the authors to account for the so-called "anamnesic response" — that is, the enhancement of antibody titers in the serums of previously immunized animals by a wide variety of unrelated stimuli, as well as by such toxic substances as benzene and potassium arsenite.

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MASSACHUSETTS MEDICAL SOCIETY

PROCEEDINGS OF THE COUNCIL

Special Meeting, October 2, 1946

A STATED meeting of the Council was called to order by the president, Dr Dwight O'Hara, Middlesex South, on Wednesday, October 2, 1946, at 10.30 a.m. in John Ware Hall, 8 Fenway, Boston. Two hundred councilors (Appendix No. 1) were present.

In opening the meeting the President read the following obituaries:

CHARLES SUMNER ADAMS — Dr Adams was born at Carlisle on October 12, 1869. He was educated at the Howe School in Billerica and at Berwick Academy. He graduated from the Harvard Medical School in 1894 and settled in Quincy the same year. In 1900 he married Frances Gertrude Monahan, who survives him, with two daughters.

Dr Adams served as vice-president of the Norfolk South District Medical Society in 1911 and 1912, and as president in 1913 and 1914. Thereafter he was continuously in the service of the Society until his death. He was alternate nominating councilor for eight years, nominating councilor for two years, councilor for twenty-one years and supervising censor for twenty-one years. His death was said to be due to carcinoma of the intestine.

HENRY MAYOR LANDESMAN — Dr Landesman was born in 1884 and graduated from the College of Physicians and Surgeons in Boston in 1917, being licensed to practice the same year in Massachusetts. He was a councilor for the Norfolk District Medical Society from 1935 to 1940 and from 1944 until his death. Between 1937 and 1944 he served as secretary of the Committee on Automobile Insurance Claims. He was sixty-one years of age at the time of his death.

WILLIAM D'ARCY KINNEY — Dr Kinney was born in 1873 and received his medical degree from Bowdoin Medical School in 1899. He had practiced in Osterville for nearly half a century. He was president of the Barnstable District Medical Society from 1913 to 1915, commissioner of trials from 1915 to 1919 and a censor in 1912 and 1913 and from 1916 to 1919. He was a supervising censor from 1922 to 1946 and a member of the Council from 1919 to 1946. He was a member of the Nominating Committee from 1922 to 1946, a member of the Executive Committee of the Council from 1941 to 1945, an alternate member in 1945 and 1946, a member of the Committee on Public Relations from 1942 to 1946 and representative to the Massachusetts Central Health Council from 1930 to 1946. Dr Kinney was associate medical examiner for Barnstable County for a period of about twenty years. His widow and a son survive him.

Although Dr Kinney was not actually a member of the Council at the time of his death on July 12, he had been active in its affairs for nearly thirty years and he will be widely recalled as an unusually faithful, interested and helpful fellow of the Massachusetts Medical Society.

WALTER HALL PULSIFER — Dr Pulsifer of Whitman, died on September 26. He was born in 1883. He graduated from Tufts College Medical School in 1908 and joined the Massachusetts Medical Society in 1910. Throughout his professional life he was especially interested in pediatrics. Dr Pulsifer was a censor from 1926 to 1927 and again in 1929. He was commissioner of trials for the years 1930 and 1931, a councilor and a member of the Nominating Committee from 1937 to 1944, inclusive, and during 1944 was a member of the special committee that was asked to look into the possibility of better publicity for the Massachusetts Medical Society. In 1945, Dr Pulsifer

was elected vice-president of the Plymouth District Medical Society and this year was elected president of that district society, holding this important office, and by virtue of it being a vice-president of the Massachusetts Medical Society, at the time of his death.

At the request of the President, the Council stood for one minute in silent tribute to the memory of these deceased councilors.

The Secretary submitted the record of the annual meeting of the Council held on May 21, 1946, as published in the *New England Journal of Medicine*, issue of September 12, 1946, and moved its adoption. This motion was seconded by Dr John Homans, Suffolk, and it was so ordered by vote of the Council.

REPORTS OF COMMITTEES

Executive Committee — Dr Michael A. Tighe, Middlesex North, secretary.

The Secretary submitted this report, which is as follows, as published in the "Circular of Advance Information" and moved its acceptance.

The Executive Committee of the Council held its pre-Council meeting on September 4, 1946, at 4:00 p.m., at 8 Fenway, Boston. The committee processed the following committee reports:

Committee on Arrangements

The Executive Committee noted that this report contains two recommendations that the annual meeting be held in Boston on May 20, 21 and 22, 1947, and that the meeting be increased in length from two and a half to three days.

The Executive Committee recommends that the Council adopt these recommendations.

Committee on Legislation

The Executive Committee, in recommending the acceptance of this report, notes that it is primarily one of information. It contains no recommendations.

The Executive Committee would particularly direct the attention of the Council to that part of the report which indicates that the members of the General Court are becoming increasingly co-operative with the Massachusetts Medical Society in its efforts toward maintaining high standards of medical practice in the Commonwealth. It further notes that this report gives much of the credit for this state of affairs to Mr. Charles Dunn, legislative counsel. The Executive Committee would include in this same category the chairman, the members of the committee and all those who have extended much well directed effort toward this same end.

Committee on Public Relations

The Executive Committee regards this report as largely informational. It notes, however, a few lines that are in the character of a recommendation. This recommendation would refer to the Massachusetts Hospital Association certain financial difficulties which have arisen between hospitals and insurance companies. This matter came originally to the Council's attention by means of certain

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issue a questionnaire to every member of the Society based on the wishes of the Council

It was pointed out that this questionnaire would go only to members of the Society, not because there was any desire to exclude others from this program but because there was no other list of physicians available

The Executive Committee next turned its attention to the third question which the committee propounded "What formula shall be used whereby the fees paid to the specialist shall be differentiated from those paid to the general practitioner?" The suggestion of the committee presenting this report is that the schedule of fees adopted by the Council on April 10, 1946 be regarded as specialists' fees and that when the services called for in this schedule are rendered by general practitioners the compensation shall be 20 per cent less than that set forth in the schedule

The Executive Committee recommends that the Council adopt this formula. The Executive Committee notes that the committee asks for a leeway not to exceed 5 per cent, so the fees finally set down for the general practitioner may appear in round numbers

The Executive Committee also recommends that the Council adopt this proposal

The report speaks of the action of the Council on April 10, 1946, whereby the Blue Shield was designated as the administrative agent for this veterans' medical-care plan in Massachusetts. The committee now recommends that this action be rescinded

It was explained that the Medical Service Administration of New Jersey operated a medical-care plan for the veterans identical with that adopted by the Council on April 10 and that New Jersey's experience with this plan was rather distressing

This experience can best be stated by reading into this record a letter received from Dr. Norman M. Scott, medical director of the New Jersey plan, by the Secretary

July 25 1946

Dear Dr. Tighe

This will acknowledge receipt of your letter dated July 15 relative to care of the veteran

I almost hesitate to write of our experience for fear of being misunderstood

The Medical Society of New Jersey, and the physicians of New Jersey as a whole are anxious to fulfill any obligation they have toward the veteran in the care of his service connected disabilities. The problem reduces itself to definition of the obligation of the profession and the means of fulfilling this obligation

The Society has organized two nonprofit medical service corporations: Medical Service Administration of New Jersey and Medical-Surgical Plan of New Jersey

You are probably acquainted with Medical Surgical Plan. It operates on the prepayment insurance basis providing benefits for services of private physicians rendered its subscribers who are admitted to hospital for treatment. It is similar to Massachusetts Medical Service

Medical Service Administration deals with problems of the indigent and low income group and plans which co-operate with local and federal government agencies such as the Farm Security Administration Medical Plan and the City of Newark Medical Plan for care of the indigent and medically indigent of the city. It is a small administrative organization. It appeared to be the logical agency in New Jersey to deal with the veterans problem. In fact we could not use our larger organization, Medical-Surgical Plan, because of the chance of jeopardizing the subscription funds of our subscribers.

In February 1946 Medical Service Administration entered into what we considered a very simple contract with V. A. We agreed that all authorizations for medical care of the veteran would be issued through our office that physicians' reports would be returned through our office and that we would bill the V. A. at intervals for authorized services rendered. We had special agreements with our 3000 physicians to render the services and a fee schedule acceptable to the majority of physicians. The Society advanced us \$10,000 to place the plan in operation

We operated the plan until May 15 1946. Some of our difficulties were as follows:

1. The load was heavier than we had anticipated. We processed an average of 300 claims a day. The return of reports from physicians rose as high as 248 on one day. The recording of all these details in our records required a lot of detail clerical work. For instance it took the time of two clerks to open and sort the mail. Telephone messages from physicians and veterans were very heavy.

2. We developed a force of twelve typists and one male executive assistant. It is difficult to train girls to do this work and to acquaint them with such subjects as medical nomenclature and methods of properly posting medical records. These twelve girls were able to handle 300 cases a day plus the incoming reports. These 300 cases were mostly treatment cases. In addition we processed about 50 physical examination cases a day averaging 3 examinations per case. We never were able to process the full number of physical examination cases referred to us and on May 15 had a backlog of about 1000 physical examination cases unprocessed.

3. As an example one type of treatment case proved very difficult to administer. A physician in a small town would request us say eight office visits, a gastrointestinal x-ray series, blood chemical studies and a gastric analysis, or a group of similar diagnostic services in a case under his care. The authorization would be issued to us in the name of the doctor in the small town who had no facilities for rendering such services. V. A. insisted that all such authorizations be billed them as one authorization and that any part of the authorization not included in our billing be canceled. This meant that we had to issue the authorization to the small town physician have him refer the case to a proper consultant, obtain the reports of consultants and include them with his report at the end of the month. We would then bill V. A. and pay the general practitioner for all services and he in turn would pay the consultants. Physicians do not like this method it is not within the framework of private medical practice. Or we could split up the authorization in this office and distribute it to the various consultants with a notice that they return their reports to us and a copy to the general practitioner. We would then wait until all reports contained in the authorization were received in this office so we could bill V. A. under one item. The trouble with this method was that the veteran would not report for certain of the examinations or the consultant would neglect to render his report promptly and we would have to follow it up by letter or if we did bill V. A. for the reports received and later a consultant rendered a report it would not be payable as the authorization had been terminated and the item closed in the V. A. finance department when the first reports were received. It is complications such as these which give administrators gray hairs.

4. We had trouble finding sufficient office space and finally wound up with offices in three different buildings in the city.

I have outlined above a few of our difficulties. These are administrative difficulties which could have been overcome in time and were not the main reason for changing our contract.

In operating the plan we simply received authorizations from the Regional Office and retyped these authorizations on our own forms and forwarded them to the physicians designated in the authorizations. This applied to treatment authorizations. The physical examination authorizations bore no physician's name and the examinations were delegated by us to a general practitioner or specialist capable of performing the examination requested. In other words we were a fifth wheel which delayed rather than expedited the rendering of care to the veteran. We had no control over the volume of the type of care rendered or the standards of medical care except to determine that the services were rendered by fully licensed physicians. We were just repeating work already done by the Regional Office.

Billing the V. A. was a formidable effort. They must be billed in each case according to claim number of the veteran his name date of the authorization date of each service each item of service cost of each service and total. This makes a long voucher especially when done without proper equipment. Our largest voucher covering a period of two weeks was 91 pages long. These vouchers are inspected and compared with the authorizations item by item in the medical division of the V. A. Regional Office. The inspection of the 91 page voucher mentioned above consumed about eighteen days. When approved by the medical division the vouchers are forwarded to the finance division where the inspection is repeated by comparison with the copies of authorizations retained by the finance officer. Vouchers then go to the procurement division and finally are forwarded to the Treasury Department in New York for payment. The result is a delay in payment. We have been paid on one voucher covering physicians' reports received between March 15 and 0 totaling about \$700 of which our administrative allotment was \$35. This is our total income to date although we must still maintain and support a skeleton organization to complete this work at the expense of the Society. Our outstanding vouchers have a value of about \$75,000 which we know will eventually be paid, of which our administrative allotment is about \$5,500.

To have continued the plan would have cost the Society many thousands of dollars which we did not feel was warranted even though we thought there was a fair chance of being able to reimburse it at least in part.

I think there is an advantage in having a recognized agency of each state society involved in the administration of the plan. Many of the men have expressed the opinion that they would rather deal through our office than directly with the Regional Office and that they liked our administrative procedure better. It is apparently working satisfactorily in Michigan through Michigan Medical Service and in California through California Physicians Service. They are both large organizations with complete modern accounting facilities and with sufficient trained personnel to absorb the load. The setup of Massachusetts Medical Service under the able administration of Mr. Cahalane and Dr. Hayden should be able to do a much better job than we did. The men in Massachusetts would perhaps rather work through them than directly with V. A. but I still feel the work of Massachusetts Medical Service would be almost entirely limited to that of a distributing agency for V. A.

This brings me back to a denouement of the obligation of the profession to the veteran. It seems to me that if the majority of physicians agree to render service to the veteran at fees agreed on by the majority and participate conscientiously in the program we have fulfilled our obligation. It should not be necessary for the profession to assume responsibility for administrative matters. V. A. does however need our administrative assistance and advice. On this promise we changed our contract. I am enclosing a copy of the new contract and the preliminary edition of an article just dictated to appear in our August journal.

It is all a new problem a difficult problem for both V. A. and the profession. Difficult administrative problems will arise and continue to arise until the best solution of the entire problem is evolved. We are much interested in the problem and will be interested in the solution promoted by your society.

Yours very truly

[Signed] NORMAN M. SCOTT
NORMAN M. SCOTT, M.D.
Medical Director

letters which the Secretary received from Dr. Shields Warren. These letters were referred to the Committee on Public Relations at the direction of the Council.

The Executive Committee recommends the adoption of the recommendation.

Subcommittee on Labor and Industry

The Executive Committee recommends the adoption of the recommendation that this subcommittee be discontinued.

Committee on Postwar Planning

The Executive Committee notes that this report contains two recommendations.

The first is that the Council create a special committee to be known as the Committee on Emergency Medical Service. In the discussion attending this subject before the Executive Committee, it came out that this matter was originally referred by the Council to the Committee on Postwar Planning. It came to the Council's attention through a letter, which had been received from Dr. Edward Bortz, requesting the formation of a committee within the Massachusetts Medical Society, which committee would be expected to collaborate with a similar committee authorized by the House of Delegates of the American Medical Association and headed by Dr. Bortz. The purpose was to study the medical resources of the country and how best to mobilize them in times of war or other disaster.

The Executive Committee noted in connection with this recommendation that the Postwar Planning Committee expressed its belief that, in the naming of the personnel of such a committee, attention should be paid to utilizing the experience gained in the last world war to the end that such mistakes as were made in that war might not be repeated.

It also came out in the discussion that, because the Postwar Planning Committee envisioned a time when its job would be finished whereas the work of the proposed committee might go on for many years, it would be better to handle this matter through a committee set up for this special purpose.

The Executive Committee recommends the adoption of this recommendation.

The second recommendation calls on the Council to approve of the inclusion in the program of the annual meeting in 1947 adequate discussion of some topic in medical economics.

The Executive Committee approves of this recommendation and, if adopted by the Council, recommends that the matter be referred to the Committee on Arrangements.

Committee Appointed to Make a Survey of Malpractice Insurance in Massachusetts

The Executive Committee recognizes that this report is purely informational. It speaks of the study which is being conducted by this committee and of some of the things which this study is turning up. The report offers no recommendation. The committee proposes to continue the study of this important study. It will offer its recommendations to the Council at a later date.

The Executive Committee recommends that the Council accept this report as one of progress.

Medical Advisory Committee to Regional O.P.A.

This report is purely informational. It contains no recommendation. The Executive Committee recommends that it be accepted by the Council.

Committee Appointed to Meet with General Hawley with a View of Formulating a Program in Massachusetts for the Medical Care of Veterans and Their Dependents

This report indicates that if the Society is to co-operate with the Veterans Administration in this program, the Council must differentiate between the specialist and the nonspecialist, something the Society has never done before.

The committee seems fully aware of the seriousness of this problem and rightfully does not assume the responsibility for its solution.

The committee submits three questions to the Council, all of which must be answered if it is to proceed.

The Executive Committee recommends that the Council answer the first question "Shall such a differentiation be made?" in the affirmative.

With regard to the second question "How shall it be arrived at?" the Executive Committee notes that the committee offers two suggestions, the first of which would allow the individual doctor to state in which one of these two groups he should be placed. The Executive Committee notes that the report says that this is the method pursued by the New Jersey Medical Society.

In this connection there was read into the record of the meeting of the Executive Committee the following questionnaire which was sent to the members of the New Jersey Medical Society:

- | | | |
|---|--------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| 1 | I agree to participate in the Veterans Medical Care Plan as arranged between the Medical Society of New Jersey and Veterans Administration | |
| 2 | I am in general practice | |
| 3 | I am doing special work in | |
| 4 | I am confining my work entirely to | |
| 5 | I can accommodate | physical examinations per |
| | month in my office | M.D. |

The debate on this particular suggestion indicated that it left too much latitude in the hands of the individual doctor which might, however, be somewhat offset by reason of the fact that once the individual doctor had classified himself as a specialist in a particular field he would not be permitted to see patients under this program in any other field.

The Executive Committee recommends that the Council reject the first suggestion.

The Executive Committee recommends that the second suggestion be amended by the Council so that the comma between the words "boards" and "those" be deleted and the word "and" be inserted in its place to read:

To designate as specialists all those so certified by the specialty boards and those physicians who state that they limit their practice to a special field or who practice a specialty in an approved hospital as a member of that hospital's regular staff.

The Executive Committee recommends that the Council adopt this suggestion as amended.

In the debate leading to this action of the Executive Committee it was made clear that the Society will not be called on to designate specialists in the field of neurology or psychiatry. The debate also indicated that the Executive Committee believes that there are many individual physicians who by long practice in a special field have fully qualified themselves as specialists in that field even though they have for one reason or another never qualified before a specialty board. It was observed that there were those who might not see much difference between the first suggestion and that part of the second which allows a man to qualify by stating that he limits his practice to a specialty.

In this connection it was pointed out that, in the first, the doctor himself, without further qualification, says in which group he should be placed, while in the second he is asked to state the circumstance of his practice, his classification being made on this as a statement of fact. It was further explained that this qualification was included in the second so as to permit that individual to qualify as a specialist who, while devoting himself exclusively to a special field, was not a member of the staff of an approved hospital.

It was the general feeling in the Executive Committee that, if the Massachusetts Medical Society were to designate any physician as a specialist, it must have control of the circumstance under which such a designation would be made.

The Executive Committee believes that in the second suggestion such controls exist. There was no disposition in the Executive Committee to regard the controls set up in the second as perfect. They were the best that could be thought of at the moment. Time and experience might indicate the necessity of their modification at some future time.

It was explained by Dr. McCarthy, chairman of the committee having this matter in hand, that if the Council accepted these or other proposals this committee would

It was pointed out that, if success was to crown the Society's efforts in the continued fight against the federal control of medicine, it should join forces with all those who think as it does and whose goal is the same even though the paths by which that goal is reached may in some respects differ.

With such thoughts in mind, the Executive Committee recommends that these communications be referred to the Committee on Public Relations, with the suggestion that a subcommittee be set up by that committee for the purpose of the study outlined in them.

MICHAEL A. TIGHE, M.D., *Secretary*

The motion to accept this report was seconded by Dr. Walter G. Phippen, Essex South, and it was so ordered by vote of the Council.

Committee on Arrangements — Dr. Sidney C. Wiggin, Suffolk, *chairman*

This report, which is as follows, was submitted by the Chairman:

A meeting of the Committee on Arrangements was held on June 28, 1946. It was voted by the committee that it recommend to the Council that the annual meeting should be held in Boston on May 20, 21 and 22. Space has been reserved at the Hotel Statler for the meeting for these days.

It was also voted to recommend to the Council that the meeting be increased in length from two and a half to three days.

Dr. Wiggin moved its acceptance. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

The President called attention to the fact that this report contained two recommendations and announced that the Executive Committee had approved both of them. Dr. John J. Curley, Worcester North, moved the adoption of the recommendations. This motion was seconded by Dr. David Cheever, Suffolk, and it was so ordered by vote of the Council.

Committee on Legislation — Dr. David L. Belding, Norfolk South, *chairman*

This report (Appendix No. 2) was submitted by the Secretary in the absence of the chairman.

Dr. John J. Curley moved the acceptance of the report. This motion was seconded by Dr. Carl Barse, Norfolk, and it was so ordered by vote of the Council.

Committee on Public Relations — Dr. Albert A. Hornor, Suffolk, *secretary*

This report (Appendix No. 3) was submitted by Dr. Hornor.

The President called attention to the fact that this report contained one recommendation, namely, that certain financial difficulties which certain hospitals were having with insurance companies be referred to the Massachusetts Hospital Association as the agency more particularly concerned in this matter. Dr. Hornor moved the acceptance of the report and the adoption of the recommendation. This motion was seconded by Dr. James V. McHugh, Worcester North.

Dr. P. R. Withington, Norfolk, expressed the thought that the doctor did have a concern in this

matter inasmuch as the doctor needed the hospital quite as much as the hospital needed the doctor.

The President pointed out that this matter was fully discussed in the Committee on Public Relations and that, inasmuch as the committee was not aware of the details of this controversy, it would be much better to refer the matter to the Massachusetts Hospital Association as the organization most fitted to deal with it. The President added that the Executive Committee had approved of the recommendation. This motion was adopted by vote of the Council.

Subcommittee on Labor and Industry — Dr. Daniel B. Reardon, Norfolk South, *chairman*

The report, which was offered by the chairman, is as follows:

I have felt for some time that the Subcommittee on Labor and Industry had fulfilled its obligations and I can see no reason why it should be continued. Therefore, I recommend that this subcommittee be discontinued.

Dr. McHugh moved the acceptance of the report and the adoption of the recommendation. This motion was seconded by Dr. Phippen, and it was so ordered by vote of the Council.

Committee on Postwar Planning — Dr. Howard F. Root, Suffolk, *chairman*

This report, which is as follows, was presented by Dr. Root:

The president of the Society sent to the chairman of the Postwar Planning Committee a communication from the headquarters of the American Medical Association in June regarding the formation of a committee designed to consider the utilization of medical services in any future national emergency. The chairman of this committee is Dr. Edward Bortz, of Philadelphia. A consideration of this matter was turned over to the Subcommittee on Veterans Affairs, and as a result of their report, the committee believes that the Council should take some action in relation to this important affair. A letter from the chairman of the national committee, Dr. Bortz, states that one objective of this committee is to secure from all medical officers who served in World War II a statement regarding their assignment. The committee recommends that the Council direct the President to appoint a Committee on National Emergency Medical Service and to include in its membership sufficient representation of those with special experience in the last world war.

The committee considered reports from the American Medical Association meeting at San Francisco, and particularly the increasing importance of certain economic and legal aspects of modern medicine. The committee recommends that the Council approve the inclusion in the program for the annual meeting in 1947 adequate discussion of some topic in medical economics.

The program for postgraduate instruction in various centers in the Commonwealth has been prepared and will be carried out with the co-operation of local committees through the fall and winter.

Dr. Root submitted a supplementary report, which was informational only and concerned itself with a suggested plan whereby a postgraduate clinical program to be held in the Boston hospitals might be combined with the annual meeting. He added that the details of the plan, which were still in the discussive stage, would be reported on later when and if they matured.

Also read into this record are the salient points of the new contract entered into by the Medical Service Administration of New Jersey with the Veterans Administration. These are as follows:

The new contract provides that Medical Service Administration will engage one or more competent medical representatives to be stationed at and operate from the Veterans Administration Regional Office.

The functions of this medical representative (or representatives) in brief shall be: (1) To certify a list of competent physicians throughout the State to render examinations and treatments to veterans. (2) To review the work of these physicians to the end that examinations and treatments are adequate, satisfactory and in accordance with established standards. (3) To make such investigations as Veterans Administration may request concerning complaints, deficiencies or inadequacies of reports made by examiners and to submit reports and recommendations thereon to Veterans Administration and Medical Service Administration. (4) To serve as liaison officer between Veterans Administration and Medical Service Administration but not as a supervisor of Veterans Administration activities or employees.

Veterans Administration will provide office space, equipment, clerical assistance and telephone service.

Veterans Administration will pay Medical Service Administration \$10,000 a year, payable quarterly in arrears, but the amounts so paid shall not exceed the amounts expended or incurred by Medical Service Administration.

The following comments made by New Jersey on this new plan were likewise read into the record:

Under the new plan authorizations for examinations and treatments will be issued directly from the Regional Office of Veterans Administration to the physician. The list of over 3000 participating physicians, in accordance with their type of practice, maintained under the previous plan will be continued. The fees paid physicians will remain the same as under the previous plan.

The new plan we believe will prove much more satisfactory than the first plan. It should expedite the medical care of the veteran and protect the interest of the private practitioner of medicine.

It must, however, be remembered that the administrative phase in providing medical care of service-connected disabilities among the 600,000 veterans of New Jersey by private physicians is a formidable problem. It is a new problem for both the profession and Veterans Administration, and that difficult administrative problems will arise and must continue to arise until a satisfactory solution for the entire problem is evolved. It is the sincere hope of Medical Service Administration that the problem will be satisfactorily met by the voluntary co-operation of the profession.

The committee in charge of this work looks upon the new contract which New Jersey has entered into as a modification of the Kansas Plan, which was fully explained at the meeting of the Council on April 10, 1946.

It now recommends that the Council approve the Kansas Plan so modified as to provide that the Blue Shield shall act as the liaison between the Veterans Administration and the physicians rendering this service in Massachusetts.

The Executive Committee recommends that the Council rescind its action of April 10, 1946, as previously outlined.

With regard to the second recommendation of the committee, the Executive Committee inquired whether or not the Blue Shield had been consulted in this matter. The chairman of the committee in charge of this work replied that it had and that it was in accord with the recommendation. The Secretary expressed the thought that, if the accord was in writing, it would clear the air and obviate the necessity of considerable debate before the Council.

In this connection the following letter was received:

MASSACHUSETTS MEDICAL SERVICE

September 18, 1946

Dwight O'Hara, M.D. President
Massachusetts Medical Society
8 Fenway
Boston, Massachusetts

Dear Doctor O'Hara:

In order that the Massachusetts Medical Society may be officially aware of the attitude of the Blue Shield Board of Directors relative to the Veterans Administration's proposed medical-care program, there are quoted below excerpts from minutes of meetings of the Blue Shield Board of Directors at which this matter was considered.

January 9, 1946—"Dr. Humphrey L. McCarthy presented to the Board a detailed explanation of the plans of the Veterans Administration for the care of veterans of World War II and discussed various plans under which the corporation might render assistance and participate in providing medical care for such veterans. It was the opinion of the directors that the corporation should co-operate with the Veterans Administration in every possible way provided that the financial stability of the corporation was not affected thereby."

April 10, 1946—"Voted that Dr. Hayden, the medical director, and Mr. Twomey, the attorney for the corporation be authorized to negotiate a contract with the Veterans Administration for the furnishing of medical and surgical service to disabled veterans and that Dr. Hayden, the Medical Director, be authorized to execute such contract on behalf of the corporation."

Respectfully,

[Signed] CHARLES G. HAYDEN
CHARLES G. HAYDEN, M.D.
Medical Director

The Executive Committee took no action on this recommendation pending the Council's action on the committee's first recommendation. The disposition of the Executive Committee, however, seemed favorable to this second recommendation provided the first recommendation was adopted by the Council and provided the Blue Shield was favorably disposed toward it.

Committee to Study the Revision of the Salaries of the Employees of the Society

The Executive Committee recommends that the Council adopt this report and the recommendations contained in it.

Committee on Finance

The Executive Committee notes that this report approves the recommendations called for in the previous report. It also approves of an additional appropriation of \$900 to cover the expenses of our representatives to the meeting of the House of Delegates of the American Medical Association to be held in Chicago in December, 1946. It was explained that this item was not covered in the annual budget because at that time there was no knowledge that such meeting of the House of Delegates of the American Medical Association was to be held.

The Executive Committee recommends that the Council adopt the recommendations contained in the report.

Committee on Postgraduate Assembly

In connection with this report the Executive Committee in a special manner directs the Council's attention to an implication which might be read in certain lines, namely, that monies taken in by the Society in a manner indicated in the report may be earmarked with regard to their expenditure. The Executive Committee points out that this may not be done. In support of this view, it quotes Chapter VI, Section 5, of the by-laws.

The Executive Committee recommends the acceptance of this report provided the provisions of Chapter VI, Section 5, are strictly adhered to.

Committee to Meet with the Massachusetts Hospital Association

This is an informational report. The Executive Committee recommends its acceptance.

Report of the Massachusetts Representatives to the House of Delegates of the American Medical Association

This report, which was prepared by Dr. D. Scannell, is informational. It is exceptionally well done. The Executive Committee recommends that the members of the Council read it carefully.

COMMUNICATIONS

The Executive Committee notes that the first two of these communications deal with the same subject. The John Hancock Mutual Life Insurance Company and the Liberty Mutual Insurance Company join in a request that the Massachusetts Medical Society set up a committee for the purpose of passing on the merits of individual sickness insurance plans as offered by old-line insurance companies.

These letters indicate that the inspiration, which directed them to be sent at this time to the President, rose out of the policy adopted by the House of Delegates of the American Medical Association at its San Francisco meeting. This policy had to do with a change of name whereby the Council on Medical Service and Public Relations is to be henceforth known as the Council on Medical Service and its function limited to a study of all types of insurance whose purpose is to meet the medical-care costs of sickness. This council will give its approval to any plan for this purpose which meets the standards which it will set and provided that the plan in question is first approved by a constituent state medical society.

The debate in the Executive Committee seemed to indicate that, although the Society through the Blue Shield is committed to insurance based on the medical-service principle as the best way to meet the medical-care costs of the low-income group, and, although it should continue to emphasize this principle, it should not assume opposition to other methods of insurance by means of which these costs might be met.

At this point in the proceedings, a discussion arose concerning the significance of the word "designate" as it appeared in the second suggestion. This discussion was participated in by Drs Fremont-Smith, Suffolk, and Baty, Middlesex South. The latter thought the word "define" should more properly be used. The former said that whatever language was adopted should make it clear that this step was taken for the purpose only of the Veterans Administration.

Dr Fremont-Smith moved as an amendment to the motion to adopt the recommendation of the Executive Committee that this recommendation be adopted subject to the insertion after the word "specialists," the words "for the purpose of the Veterans Administration only." This amendment was seconded by a councilor.

Dr Allan Butler, Suffolk, further amended the motion so as to provide that the word "define" be substituted for the word "designate." This amendment was likewise seconded by a councilor.

Dr Schadt asked if, after certain members were defined as specialists, those remaining were to be classified as general practitioners. The President answered in the affirmative.

The motion as amended by Dr Fremont-Smith and Dr Butler was adopted by vote of the Council.

The President said that the next matter before the Council was concerned with the third question submitted by the committee. He added that the committee suggested the following formula whereby the fees paid specialists might be distinguished from those paid the general practitioner:

The schedule of fees approved by the Council on April 10, 1946, shall be regarded as specialists' fees, and when the services called for in this schedule are rendered by the general practitioner, the compensation shall be 20 per cent less than that set forth in that schedule, with the understanding that if such a formula were adopted the committee be allowed a leeway not to exceed 5 per cent so that the fees finally set forth in the schedule shall appear in round numbers.

Dr Bagnall was recognized by the Chair. He spoke as follows:

So far as the fees are concerned, I should like to remind you that in April you adopted a fee schedule for Blue Shield to run this scheme, when it was finally adopted. I think it is fair to say that not many of you felt that the schedule of fees that was adopted was a schedule of fees that was reasonable. Due, perhaps in part at least, to the tremendous energy of the chairman of that committee, the schedule was adopted, and I had the pleasure of casting the only dissenting vote. But afterward I talked with a great many men, and I have not found but one since who thought that it was a fair fee schedule.

Now you come to the point of reducing that fee schedule by 20 per cent, which shows that the committee believes that the original fee schedule was not fair.

We could refer this schedule back to the committee, with the idea that they should make whatever adjustment the Veterans Bureau feels desirable, if it seems reasonable in the committee's point of view and if it feels that they are not letting the Society or the Council down.

It would be too big a job for the Council to go into the matter of fees again. The idea of dropping them 20 per cent for general practitioners seems fair enough. I have

not gone over the schedule on the basis of the 20 per cent reduction. I should prefer to leave it to the committee to iron out with the Veterans Administration on a basis that was mutually satisfactory.

Dr McCarthy moved the adoption of the suggestion offered by the committee. This motion was seconded by a councilor.

The President said that the Executive Committee approved the adoption of this suggestion. The motion was adopted by vote of the Council.

At that point, the Council went into executive session, from which it arose half an hour later.

The President said that the next matter before the Council was the recommendation of the committee that the Council rescind its action of April 10, 1946, whereby it was recommended that the Blue Shield be named the administrative agency in Massachusetts for the plan which concerned itself with the medical care by the civilian doctors of those for whom the Veterans Administration is responsible. The Council proceeded to discuss the matter informally.

Dr Fremont-Smith asked that a statement be made to the Council outlining the advantages and disadvantages of having the Veterans Administration set up its own administration in this state, and a further statement that would likewise outline the advantages and disadvantages of the Blue Shield's taking over the administration of this program. The President called Dr Smith's attention to the fact that the "Circular of Advance Information" told the story rather completely.

Dr Donald Munro, Suffolk, said that it was not entirely clear to him as to what the function of Blue Shield would be when and if it took over this administration. He asked if it would have any control of the fee schedule. He added that, as the result of what Dr Bagnall had said earlier in the meeting, there might be some question whether or not the Blue Shield, if they took over this administration, might want to reduce the fee schedule to the level of its own schedule. Dr Bagnall replied that he had no such thought in mind.

The President said that it was apparent that the committee made the recommendation because of the hopeless state that New Jersey got into in its attempt to administer a plan of this kind. He quoted Dr Bagnall as saying that in spite of New Jersey's difficulties the latter was of the belief that the Blue Shield could and would like to administer the plan in Massachusetts. He emphasized the fact that the Blue Shield had nothing to do with the fee schedule set up by the Council to cover medical services rendered under this program.

Dr Phippen said that it seemed clear to him that the Blue Shield was perfectly willing to go ahead with this proposition and because it was geared to handle the care of sick individuals on an insurance basis the Council would be well advised to let them handle this veterans' plan.

Dr Root moved the acceptance of the report. The motion was seconded, and it was so ordered by vote of the Council.

The President announced that this report contained two recommendations: first, that the Council direct the President to appoint a Committee on National Emergency Medical Service and to include in its membership sufficient representation of those with special experience in the last war, and secondly, that the Council approve of the inclusion in the program of the annual meeting in 1947 adequate discussion of some topic in medical economics. The President added that both these recommendations had been approved by the Executive Committee.

The first recommendation was adopted by vote of the Council on a motion by Dr Curley, seconded by Dr Phippen.

Dr Root moved the adoption of the second recommendation. This motion was seconded by Dr Curley, and it was so ordered by vote of the Council.

Dr Root moved the adoption of the report as a whole. This motion was seconded by Dr Phippen, and it was so ordered by vote of the Council.

Committee to Make a Survey of Malpractice Insurance in Massachusetts — Dr Carl Bearse, Norfolk, chairman.

This report (Appendix No. 4) was presented by the chairman. He said that it was purely informational and that, as the subject was still under investigation, no recommendations were being offered at that time.

He moved the acceptance of the report as one of progress. The motion was seconded by a councilor, and it was so ordered by vote of the Council.

Medical Advisory Committee to the Regional OPA — Dr Joseph Garland, Suffolk, chairman.

This report, which is as follows, was offered by the chairman:

The Medical Advisory Committee to the Regional OPA has met only once this year, on May 9, 1946. The main purpose of this meeting was to discuss the problems of various hospitals that had requested extra sugar. The question was referred to the Hospital Council of Boston for its advice, the result apparently being that this matter was left to the discretion of the committee.

Occasional applications for extra sugar rations for individuals have been referred to members of the committee, but otherwise its functions seem to be nearly over.

This report is offered for the information of the Council.

Dr Garland moved its acceptance. This motion was seconded by Dr Phippen, and it was so ordered by vote of the Council.

Report of the Committee to Meet with General Hawley with the View of Formulating a Program in Massachusetts for the Medical Care of Veterans and Their Dependents — Dr Humphrey L. McCarthy, Norfolk, chairman.

This report (Appendix No. 5) was presented by the chairman, who moved its acceptance. The mo-

tion was seconded by a councilor, and it was so ordered by vote of the Council.

The President called the attention of the Council to that part of the report which says that for the purposes of this program it is mandatory that the Council distinguish between the specialist and non-specialist. In this connection, he added, the Committee had posed three questions: (1) Shall such a differentiation be made? (2) If so, how shall it be arrived at? (3) What formula shall be used whereby the fees paid the specialist shall be differentiated from those paid to the general practitioner?

The President said that the Executive Committee recommended that the first question be answered in the affirmative.

A councilor moved that this differentiation be made. This motion was seconded.

Dr George L. Schadt, Hampden, asked the President if he would care to define the term "general practitioner." The President, while declining to answer this question, said that the Council might be able to arrive at the answer when it came to consider the suggestions which appeared later in this report.

Dr Hornor asked if legally the Council had any right to make such a differentiation. The President replied that any differentiation of the kind which the Council might make would have no standing under the law, that it was not intended that it should have, and that its sole purpose was to facilitate our program with the Veterans Administration.

Dr Carl Bearse said that he could not help but feel that the Council should hesitate before setting up such a differentiation. "Our method of practice," he continued, "has worked well in the past and it should work well in the future, even in so far as veterans are concerned."

On the invitation of the President, Dr McCarthy said that this differentiation was called for by the Veterans Administration and that it would have to be arrived at if the Society were to participate in the program. This motion was carried by vote of the Council.

The President said that the next question before the Council concerned itself with how this differentiation could be arrived at. In this connection, he added that the committee offered two suggestions: first, that a suitable questionnaire be submitted to each member of the Society asking him to designate in which one of the two groups he believes he should be placed, second, to designate as specialists all those so certified by the specialty boards and those physicians who state that they limit their practice to a special field or who practice a specialty in an approved hospital as a member of that hospital's regular staff. The President said that the Executive Committee recommends that the Council approve the second suggestion.

Dr Richard M. Smith, Suffolk, moved the adoption of the recommendation of the Executive Committee. The motion was seconded by a councilor.

Committee Appointed to Confer with the Massachusetts Hospital Association — Dr Walter G Phippen, Essex South, chairman

The report, which was offered by the chairman, is as follows

The material pertaining to the Gallupe Plan for furthering the usefulness of graduates of substandard schools in hospitals was sent to every hospital in the Commonwealth, together with the remarks made on this subject at the annual meeting of the Society. Otherwise there has been no activity of this committee.

The President said that this was a report of progress. It was moved that it be accepted as such. This motion was seconded, and it was so ordered by vote of the Council.

Report of the Massachusetts Representatives to the House of Delegates of the American Medical Association — Dr David D Scannell, Norfolk

This report (Appendix No 7) was submitted by the President in Dr Scannell's absence, who commented on the thorough manner in which the report had been prepared.

The Secretary said that Dr Scannell had been appointed by the speaker of the House of Delegates of the American Medical Association to a committee which had already met to study the report of Rich and Associates, with a view of presenting an analysis of it to the House of Delegates when it meets in December. He explained that at the direction of the Board of Trustees, this firm had been employed to conduct a survey as to how the public relations of the American Medical Association might be improved.

Dr Scannell's report was accepted by vote of the Council.

COMMUNICATIONS

The following letters to the President, each dealing with the same subject, were presented

JORN HANCOCK MUTUAL LIFE INSURANCE COMPANY
Home Office Boston Massachusetts
August 7 1946

Dr Dwight O'Hara, President
Massachusetts Medical Society
8 Fenway Boston Massachusetts

Dear Dr O'Hara,
Our company has for three quarters of a century had a sincere interest in the health and welfare of the people of this country. By providing, through insurance, a medium for sharing certain risks to which all men are liable but which fall unevenly on a few, we believe that we have contributed to general social stability and the improvement of our way of life.

At the recent convention in San Francisco we believe that the American Medical Association confirmed the opinion already held by a large proportion of the profession that in order to accomplish the desired protection of the public in the most rapid and efficient manner the doctors should co-operate with all reputable types of health insurance. Two approaches were outlined for determining the standards of such insurance, in so far as they relate to the practice of medicine: one a joint advisory body to be set up by the American Medical Association to study the problems inherent in this risk and the other an implied recommendation to the state societies to set up the machinery for passing on the merits of individual plans and the reciprocal responsibilities of the doctor and the insurance carrier which they involve. Our company desires to co-operate with the doctors in both these procedures.

It is our opinion that the pre-eminent position of the Massachusetts Medical Society in the councils of the profession makes it the logical leader in this field. It would give our company great satisfaction if your society would join with us in undertaking this public duty. While we cannot speak officially for any of the other insurance companies

we have reason to believe that such a move by your society would be welcomed by them and that they too would be happy to participate in the work.

We believe that the public would appreciate this constructive action.
Very truly yours
(Signed) H MAYNARD REES M D
H MAYNARD REES M D, Director
Medical Service Insurance

LIBERTY MUTUAL INSURANCE COMPANY
175 Berkeley Street Boston Massachusetts
August 7 1946

Dr Dwight O'Hara, President
Massachusetts Medical Society
8 Fenway Boston Massachusetts
Dear Dr O'Hara

We have followed closely the hearings before the Senate Committee on Education and Labor on the National Health Act of 1945. We have also been much interested in the recent proceedings of the House of Delegates of the American Medical Association at San Francisco.

We gather that the American Medical Association has not weakened in its opposition to compulsory health insurance but recognizes meanwhile that something more must be done than to oppose legislation regarded as undesirable. We understand the Association is thoroughly alive to the necessity for pushing voluntary plans for prepayment insurance to cover surgical and hospital expenses and convinced that a large enrollment in voluntary plans is essential. Will not give exclusive support to any one type of plan but will approve any plan which meets its requirements.

This action by the House of Delegates is constructive but should be implemented by action by the state societies since the national organization will act only on plans already approved at the local level. The Massachusetts Medical Society has attained a pre-eminent position among groups of doctors and has a record for achievements in the public interest. Therefore it would be most significant if your organization would take a position of leadership in this field comparable to what it has accomplished in other areas.

The problem demanding solution is how to provide enough people with prepaid surgical hospital and medical-care insurance at a sufficiently moderate price to meet the demand of the public for coverage without the necessity for Government operation in this field. It will not meet the problem merely to point out that certain plans are available; it will be necessary to take definite constructive action to design solutions that meet the needs of the people in terms of the coverage furnished and the number of people protected.

In our opinion the need of the public can be met, within the frame of the competitive enterprise system by co-operation between the doctors, employers and existing insurance facilities. The employer should be included in the formula because it is essential to have administrative supervision, improved industrial hygiene, practical provision for the practice of preventive medicine and groups large enough to reduce handling costs to a minimum. The employer-employee relationship is the keystone of the arch of production which must be increased if the economy is to enjoy improved standards of medicine, improved standards of health and improved standards of living.

Further, we believe that there should be a number of different plans available through a number of different facilities. We believe that competition among the several plans that may become available will achieve the best final results for the greatest number of people.

We are convinced that unless this problem can be met at a "public service" level by both the insurance companies and the doctors seeking a solution without regard to their selfish interests, socialized medicine will be the inevitable outcome.

Motivated by these thoughts we respectfully make the suggestion to the Massachusetts Medical Society that it consider favorably the proposition that it work to develop a plan of action under which the resources, facilities and experience of the insurance companies would be enlisted in a co-operative effort to achieve a practical solution to the need of the people for an extension of nonoccupational accident and health insurance within the framework of our existing economic society.

Very truly yours
(Signed) S BRUCE BLACK
S BRUCE BLACK, President

The President said that the Executive Committee had reviewed these communications and recommended that they be referred to the Committee on Public Relations with the suggestion that a subcommittee be set up by that committee for the purpose of the study outlined in them.

It was moved that the recommendation of the Executive Committee be adopted. This motion was seconded, and it was so ordered by vote of the Council.

Two communications received by the Secretary were presented to the Council. One (Appendix No 8) was from Dr George F Lull, secretary of the American Medical Association, and the other (Appendix No 9) was from Dr Frank H Lahey, chairman of the Directing Board, Procurement and Assignment Service.

Dr McCarthy said that at the meeting of the Executive Committee he was instructed to ascertain in writing the views of the Blue Shield in this matter, as mentioned in the report of the Executive Committee. He added that he had complied with this directive and that the letter which appeared in the report of the Executive Committee was the answer received. When he had heard of the difficulty in New Jersey, he continued, both he and Dr Tighe wrote to New Jersey and at the same time informed the Blue Shield of the difficulties in that area. He said that this recommendation in the report was inspired out of a sense of caution.

Dr Bagnall said that during the last three days of the current week the Blue Shield people all over the country planned to hold a meeting for the discussion of this subject and that undoubtedly much information on it would become available.

Dr Munro said that the Council seemed to be getting nowhere rapidly. He moved that this subject be laid on the table to be withdrawn when more information with regard to it is available. This motion was seconded, and it was so ordered by vote of the Council.

The order of the day was moved. The motion was seconded and it was so ordered by vote of the Council.

Committee Appointed to Study Revision of the Salaries of the Employees of the Society — Dr Charles J Kickham, Norfolk, chairman

In the absence of the Chairman, this report (Appendix No. 6) was presented by the President, who said that it called for an extra appropriation of \$1,332 for the purposes outlined in the report. He added that this appropriation had been approved by the Executive Committee.

Dr Lester M. Felton, Worcester, moved that the report be accepted and the recommendations contained in it adopted. The motion was seconded by a councilor. It was so ordered by vote of the Council.

Committee on Finance — Dr Robert W. Buck, Middlesex South, chairman

This report, which is as follows, was presented by the chairman.

The Committee on Finance has unanimously approved the salary increases as recommended by the special committee appointed to study this subject, such increases requiring an extraordinary appropriation in the amount of \$1,332 for the period from July 1, 1946, to December 31, 1946.

The following correspondence was submitted by the committee as a supplementary report.

August 24, 1946

Dr Robert W. Buck, Chairman
Committee on Finance
5 Bay State Road
Boston 15, Massachusetts
Dear Dr. Buck:

Dr. Tighe has called my attention to the fact that there is to be a meeting of the House of Delegates in Chicago in December of this year.

This is, of course, an item which was not anticipated at the time the budget for 1946 was passed upon. It would therefore, seem to me wise for the Committee on Finance to recommend to the Council that an extraordinary appropriation of \$500 be made to cover the expenses of the Massachusetts delegates to this meeting.

If you and your committee approve of making this request, I think a line from you to that effect would be all that is necessary. If possible, this should be in the Secretary's hands on or before next Wednesday, August 28, so that it may be mimeographed and added to the business for the October meeting.

Thanking you for consideration of this matter, I am

Sincerely yours,

[Signed] DWIGHT O'HARA
DWIGHT O'HARA, M.D., President

August 26, 1946

Dr. Michael A. Tighe, Secretary
The Massachusetts Medical Society
8 Fenway
Boston 15, Massachusetts
Dear Dr. Tighe:

Dr. O'Hara has asked that the Committee on Finance recommend to the Council that an extraordinary appropriation of \$500 be made to cover the expenses of the Massachusetts delegates to the December meeting of the House of Delegates in Chicago.

On behalf of the Committee on Finance I recommend this appropriation, although owing to the shortness of time not all of the members of the committee have yet been able to express their approval. When this approval is obtained, it will be forwarded to you.

Very truly yours,

[Signed] ROBERT W. BUCK
ROBERT W. BUCK, M.D.
Chairman, Committee on Finance

September 4, 1946

Dr. Michael A. Tighe, Secretary
The Massachusetts Medical Society
8 Fenway
Boston 15, Massachusetts
Dear Dr. Tighe:

I have received the unanimous approval of the Committee on Finance of the extraordinary appropriation of \$500 to cover the expenses of the Massachusetts delegates to the December meeting of the House of Delegates in Chicago.

Sincerely yours,

[Signed] ROBERT W. BUCK
Chairman, Committee on Finance

Dr. McCarthy moved the adoption of the report. This motion was seconded by a councilor, and it was so ordered by vote of the Council.

Committee on Postgraduate Assembly — Dr. Leroy E. Parkins, Suffolk, chairman

The report, which was offered by the chairman, is as follows:

The committee has joined with representatives of the other New England state medical societies to form an executive committee, which has appointed a program and other committees necessary to carry out the work of arranging the assembly. The program will be published in the *New England Journal of Medicine*, issue of September 12, 1946. All the speakers are distinguished members of the profession.

The symposium to be presented on the medical care of veterans in the Anglo-Saxon countries is of timely interest and importance.

On vote of the Executive Committee it was decided to hold the assembly in a hotel, also it was voted to have technical exhibits to help pay expenses for this assembly and provide funds to organize a better program for next year.

Dr. Parkins moved the adoption of the report provided that the following language appearing at the end of the report be deleted: "and provide funds to organize a better program for next year." He said that this deletion would bring the report into conformity with the views of the Executive Committee, the latter having recommended that the report be adopted, provided Chapter VI, Section 5, of the by-laws be strictly adhered to. Dr. Parkins's motion was seconded by a councilor, and it was so ordered by vote of the Council.

APPENDIX NO. 1

ATTENDANCE OF THE COUNCILORS

BARNSTABLE

P M Butterfield

W F Ryan

M A Tighe

W L Twarog

BERKSHIRE

I S F Dodd
C F Kernan
Helen M Scoville

MIDDLESEX SOUTH

E W Barron
Harris Bass
J M Baty
W O Blanchard
G F H Bowers
Madeline R Brown
R N Brown
R W Buck
E J Butler
J F Casey
C W Clark
J A Daley
H F Day
C L Derick
J G Downing
F W Gay
V A Getting
H G Giddings
Eliot Hubbard, Jr
A A Levi
A N Makechnie
R A McCarty
J C Merriam
Dudley Merrill
C E Mongan
G M Morrison
J P Nelligan
Dwight O'Hara
Fabian Packard
L S Pilcher
Max Ritvo
M J Schlesinger
E W Small
J E Vance
A L Watkins
B S Wood
Hovhannes Zovichian

BRISTOL NORTH

W H Allen
M E Johnson
W J Morse
J L Murphy
W M Stobbs

BRISTOL SOUTH

R B Butler
J C Corrigan
E D Gardner
Henry Wardle

ESSEX NORTH

E S Bagnall
R V Baketel
G J Connor
Elizabeth Councilman
N F DeCesare
H R Kurth
P J Look
G L Richardson
F W Snow

ESSEX SOUTH

D S Clark
R E Foss
C A Herrick
P P Johnson
W G Phippen
E D Reynolds
J R Shaughnessy
H D Stebbins
P E Tivnan
C F Twomey
C A Worthen

FRANKLIN

A W Hayes

HAMDEN

E P Bagg
A J Douglas
E C Dubois
Adolph Franz, Jr
P E Gear
G D Henderson
Charles Jurist
G L Schadt
J A Seaman
W W Teahan

HAMPSHIRE

H A Tadgell

MIDDLESEX EAST

J L Anderson
Robert Dutton
W H Flanders
R W Layton
K L MacLachlan
M J Quinn
W F Regan
R R Stratton
J M Wilcox

MIDDLESEX NORTH

R L Drapeau
D J Ellison
A R Gardner

NORFOLK SOUTH

F A Bartlett
Harry Braverman

Frederick Hinchliffe

E K Jenkins
N R Pillsbury
D B Reardon
H A Robinson
R G Vinal

PLYMOUTH

J C Angley
A L Duncombe
H H Hamilton
P H Leavitt
R C McLeod
G A Moore
B H Peirce

SUFFOLK

H L Albright
A W Allen
W H Blanchard
W J Bricklev
W E Browne
A M Butler
A J A Campbell
David Cheever
J F Conlin
Pasquale Costanza
Maurice Fremont-Smith
Joseph Garland
John Homans
A A Hornor
L M Hurxthal
H A Kelly
R I Lee
C C Lund
Donald Munro
F R Ober
F W O'Brien
J P O'HareL E Parkins
Helen S Pittman
J H Pratt
W H Robey
H F Root
R M Smith
Augustus Thorndike
J J Todd
S N Vose
Conrad Wesselhoeft

WORCESTER

C R Abbott
A W Atwood
F P Bousquet
J J Cohen
G R Dunlop
W J Elliott
John Fallon
L M Felton
R H Goodale
Thomas Hunter
H L Kirkendall
J A Lundy
D K McCluskey
J M Olson
F A O'Toole
R S Perkins
E L Richmond
N S Scarcello
J J Tegelberg
G C Tully
B C Wheeler

WORCESTER NORTH

H C Arcy
J J Curlev
J V McHugh
J G Simmons

APPENDIX NO. 2

REPORT OF THE COMMITTEE ON LEGISLATION

In the field of federal legislation a statement of the attitude of the Massachusetts Medical Society on Senate 1606 was sent by the special Subcommittee on Federal Legislation (Drs. Reginald Fitz, E S Bagnall, Dwight O'Hara, M A Tighe and J C McCann), to the United States Senate Committee holding hearings on this bill. This statement outlined the basic principles of adequate medical care as adopted by our society. It pointed out the shortcomings of Senate 1606, and gave reasons for disapproving the bill. This subcommittee continues to function in all matters pertaining to federal legislation.

In the field of state legislation, the end of the 1945-1946 session of the General Court brought a successful conclusion to our efforts. A total of eighty-four bills were considered, of which thirteen were approved and sixteen opposed. A brief statement of the disposal of some of the more important bills may be of interest.

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The President said that these letters were informational and required no action by the Council

APPOINTMENTS

The President then announced the following *ad interim* appointments

To the Council

- Dr Fred A Bartlett, Norfolk South, to take the place of Dr Charles S Adams, deceased
- Dr Joseph H Carey, Norfolk, to take the place of Dr Henry M Landesman, deceased
- Dr Franklyn P Bousquet, Worcester, to take the place of Dr John J Dumphy, resigned
- Dr Eugene L Richmond, Worcester, to take the place of Dr Gordon Berry, resigned

To the Board of Censors

- Dr Fred A Bartlett, Norfolk South, as supervisor, to take the place of Dr Charles S Adams, deceased
- Dr Paul P Henson, Barnstable, as supervisor

To the Executive Committee of the Council

- Dr Franklyn P Bousquet, Worcester, as alternate, to take the place of Dr John J Dumphy, resigned

To the Committee on Membership

- Dr Samuel N Vose, Suffolk, as chairman *pro tempore*, to take the place of Dr Harlan F Newton, resigned
- Dr Peirce H Leavitt, Plymouth, as chairman, to take the place of Dr Vose
- Dr Lewis S Pilcher, Middlesex South

To the Committee on Nominations

- Dr Franklyn P Bousquet, Worcester, as alternate, to take the place of Dr John J Dumphy, resigned

To the Committee to Confer with the Massachusetts Farm Bureau Federation

- Dr Elmer E Thomas, Hampshire, to take the place of Dr Joseph D Collins, resigned

To the Committee to Confer with the Massachusetts Hospital Association

- Dr Nicholas S Scarcello, Worcester, to take the place of Dr John Fallon, resigned

To the Committee on Postpayment Medical Care

- Dr Elmer E Thomas, Hampshire, to take the place of Dr Joseph D Collins, resigned

To the Committee on Tax-Supported Medical Care

- Dr Thomas Hunter, Worcester, as chairman, to take the place of Dr John J Dumphy, resigned

To the Committee to Meet with General Hawley

- Dr James K Bragger, Norfolk, to take the place of Dr John J Dumphy, resigned

To the Committee to Study Revision of Salaries of Employees of the Society

- Dr Charles J Kickham, Norfolk, chairman
- Dr Robert W Buck, Middlesex South
- Dr Robert N Nye, Suffolk

To the Committee to Study the Income Level of Blue Shield

- Dr Charles F Wilnsky, Suffolk, chairman
- Dr Norman H Bruce, Middlesex South
- Dr Raoul L Drapeau, Middlesex North
- Dr Henry L Kirkendall, Worcester
- Dr John W Spellman, Norfolk

To the Committee to Study Increase in Assessment of Dues

- Dr Frank R Ober, Suffolk, chairman
- Dr N Newall Copeland, Berkshire

- Dr Edwin D Gardner, Bristol South
- Dr Kenneth L MacLachlan, Middlesex East
- Dr John W McKoan, Worcester

To the Subcommittee on National Legislation

- Dr Elmer S Bagnall, Essex North, chairman
- Dr Reginald Fitz, Suffolk
- Dr James C McCann, Worcester
- Dr Michael A Tighe, Middlesex North

To the Subcommittee on Veterans Affairs

- Dr Charles Bradford, Suffolk
- Dr Stephen Brown, Hampshire
- Dr William M Carr, Plymouth
- Dr Leo R Desmond, Norfolk
- Dr Spencer C Flo, Franklin
- Dr Merrill F Gardner, Bristol South
- Dr Willis N Gowen, Middlesex East
- Dr Leonard W Hill, Bristol North
- Dr Sheldon L Hunt, Barnstable
- Dr Thomas Hunter, Worcester
- Dr John C McGirr, Middlesex South
- Dr Frank P Morse, Jr, Essex South
- Dr F K Paddock, Berkshire
- Dr Ensio K F Ronka, Norfolk South
- Dr Louis B Simard, Essex North
- Dr Thomas J G Tighe, Middlesex North

To the Council of the New England State Medical Societies

- Dr Norman A Welch, Norfolk, to take the place of Dr Dwight O'Hara, resigned

In reference to the Committee on Veterans Affairs, Dr Curley asked who represented Worcester North. The President said he would look this matter up after the meeting and let Dr Curley know. Dr Curley said he asked the question because as the list was read there was no one accredited to that district. The President said he would correct that situation within twenty-four hours.

The President's appointments were confirmed by vote of the Council.

NEW BUSINESS

Dr Bagnall moved that the committee appointed to meet with General Hawley with a view of formulating a program in Massachusetts for the medical care of veterans and their dependents be reorganized so as to consist of five members among whom would be adequate representation of the Blue Shield. This motion was seconded.

There was some discussion whether or not the motion should be referred, under the Council rules, to the Committee on Public Relations. Dr Hornor expressed the thought that it should be so referred on the basis that the committee in question was a subcommittee of the Committee on Public Relations. Dr McCarthy said that this committee was a special committee.

The President ruled that the motion would not be put to the Council, and in so ruling he said that it was within his province to act on the subject matter of the motion without a formal vote by the Council. The Council acquiesced in the ruling. There being no further business before the Council, the President announced it adjourned at 12 50 p m.

MICHAEL A TIGHE, Secretary

APPENDIX NO 1

ATTENDANCE OF THE COUNCILORS

BARNSTABLE

P M Butterfield

W F Ryan

M A Tighe

W L Twarog

BERKSHIRE

I S F Dodd
C F Kernan
Helen M Scoville

MIDDLESEX SOUTH

E W Barron
Harris Bass
J M Baty
W O Blanchard
G F H Bowers
Madelaine R Brown
R N Brown
R W Buck
E J Butler
J F Casey
C W Clark
J A Daley
H F Day
C L Derick
J G Downing
F W Gay
V A Gettings
H G Giddings
Eliot Hubbard, Jr
A A Levi
A N Makechnie
R A McCarry
J C Merriam
Dudley Merrill
C E Mongan
G M Morrison
J P Nelligan
Dwight O'Hara
Fabyan Packard
L S Pilcher
Max Rivro
M J Schlesinger
E W Small
J E Vance
A L Watkins
B S Wood
Hovhannes Zovickian

BRISTOL NORTH

W H. Allen
M. E. Johnson
W J Morse
J L Murphy
W M Stobbs

BRISTOL SOUTH

R. B. Butler
J C Cornigan
E. D. Gardner
Henry Wardle

ESSEX NORTH

E. S. Bagnall
R. V. Baketel
G J Connor
Elizabeth Councilman
N F DeCesare
H. R. Kurth
P J Look
G L Richardson
F W Snow

ESSEX SOUTH

D S Clark
R. E. Foss
C. A. Herrick
P P Johnson
W G Phippen
E. D. Reynolds
J R. Shaughnessy
H. D. Stebbins
P. E. Tivnan
C F Twomey
C. A. Worthen

FRANKLIN

A W Hayes

HAMFDEY

E. P. Bagge
A J Douglas
E. C. Dubois
Adolph Franz, Jr
P E Gear
G D Henderson
Charles Junst
G L. Schadt
J A Seaman
W W Teahan

HAMPSHIRE

H A Tadgell

MIDDLESEX EAST

J L Anderson
Robert Dutton
W H. Flanders
R. W. Layton
K L. MacLachlan
M J Quinn
W F Regan
R R Stratton
J M Wilcox

MIDDLESEX NORTH

R. L. Drapeau
D J Ellison
A R Gardner

Frederick Hinchliffe

E K Jenkins

N R Pillsbury

D B Reardon

H A Robinson

R G Vinal

PLYMOUTH

I C Angley
A L Duncombe
H H Hamilton
P H Leavitt
R C McLeod
G A Moore
B H Peirce

SUFFOLK

H L Albright
A W Allen
W H Blanchard
W J Brickley
W E Browne
A M Butler
A J A Campbell
David Cheever
J F Conlin
Pasquale Costanza
Maurice Fremont-Smith
Joseph Garland
John Homans
A A Hornor
L M Hurxthal
H A Kelly
R I Lee
C C Lund
Donald Munro
F R Ober
F W O'Brien
J P O'Hare

L E Parkins

Helen S Pittman

J H Pratt

W H Robey

H F Root

R M Smith

Augustus Thorndike

J J Todd

S N Vose

Conrad Wesselhoeft

WORCESTER

C R Abbott
A W Atwood
F P Bousquet
I J Cohen
G R Dunlop
W J Elliott
John Fallon
L M Felton
R H Goodale
Thomas Hunter
H L Kirkendall
J A Lundy
D K McCluskey
J M Olson
F A O'Toole
R S Perkins
E L Richmond
N S Scarcello
J J Tegelberg
G C Tully
B C Wheeler

WORCESTER NORTH

H C Arey
J J Curley
J V McHugh
J G Simmons

APPENDIX NO 2

REPORT OF THE COMMITTEE ON LEGISLATION

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NORFOLK

A A Abrams
B E Barton
Carl Bearse
J H Cauley
D J Collins
G L Doherty
Albert Ehrenfried
H M Emmons
Susannah Friedman
J B Hall
H B Harris
R J Heffernan
P J Jakmauh
I R Jankelson
C J E Kickham
D L Lionberger
D S Luce
H L McCarthy
Hyman Morrison
J J O'Connell
W R Ohler
G W Papen
H A Rice
J A Seth
J A Sieracki
S L Skvirsky
E C Smith
Kathleyn S Snow
J W Spellman
A R Stagg
W J Walton

NORFOLK SOUTH

F A Bartlett
Harry Braverman

chusetts students are now provided for, all future legislation directed against the Approved Act may be successfully opposed.

A bill (H 1822), which exempted veterans from legislation enacted since September 16, 1940, in respect to boards of registration and which adversely affected the Approval Act, was reported out of a conference committee of the Senate and House, with the section applying to the professions deleted. With this deletion the bill was passed by the Legislature to become Chapter 577 of the Acts of 1946.

Of the four bills (S 404, S 405, and S 406 and S 407) to revoke the charters of nonfunctioning or substandard medical schools, only S 407, which revoked the charter of the College of Physicians and Surgeons as of 1949, was passed.

A bill (H 230), initiated by Dr. Gallupe, of the Massachusetts Board of Registration in Medicine, was passed. This bill enables Massachusetts to have license reciprocity with other states.

The attitude of the members of the General Court toward the Massachusetts Medical Society is becoming increasingly co-operative. Most legislators now realize that our efforts are directed toward maintaining high standards of medical practice as an important means of safeguarding the public health. Much of this goodwill may be attributed to the well directed educational efforts of our legislative counsel, Mr. Charles Dunn.

DAVID L. BELDING, *Chairman*

APPENDIX NO 3

REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The Committee on Public Relations recommended that the President appoint a representative of the Massachusetts Medical Society to help the Academy of Pediatrics survey of facilities and need for facilities in the care of children. This question had been referred to the Committee on Public Relations by the Council of the Massachusetts Medical Society at its meeting on May 21, 1946. After the adoption of the motion President O'Hara announced that he would appoint Dr. David Sherwood as representative of the Massachusetts Medical Society to help the proposed survey of the Academy of Pediatrics.

The Committee on Public Relations accepted, with thanks, Dr. Ellison's report as chairman of the Subcommittee to Consult with the Advisory Committee of the Industrial Accident Board and this report has since been circularized to the members of the Massachusetts Medical Society.

The question of having a Woman's Auxiliary to the Massachusetts Medical Society was referred back for further investigation to the subcommittee appointed to study this question.

The Committee on Public Relations discussed the letter submitted by Dr. Shields Warren, of the New England Deaconess Hospital, in protest against the paying by insurance companies of ward rates, since these rates are set at less than the cost of caring for the patient. After much discussion the committee decided that this is a problem for the Massachusetts Hospital Association and asked to be relieved of further duties in connection with this letter.

ALBERT A. HORNOR, *Secretary*

APPENDIX NO 4

REPORT OF THE COMMITTEE TO MAKE A SURVEY OF MALPRACTICE INSURANCE IN MASSACHUSETTS

Two meetings were held, the second was attended by the chairman of the Committee on Medical Defense. Discussions were held with representatives of several insurance companies, and considerable data were obtained from the Insurance Department at the State House.

Group malpractice insurance as such cannot be written in Massachusetts. An opinion rendered by the Attorney General in 1923 stated, "A group or blanket policy of liability insurance may not be issued to an association of dentists or physicians."

There are at least ninety-four insurance companies authorized to write malpractice insurance in this state, but no information is available at present to indicate which companies

engage in this type of underwriting. About nine companies are probably doing most of this business. The Medical Protective Company, the U. S. Fidelity and Guaranty Company, and the Lumbermen's Mutual Casualty Company probably underwrite the largest number.

We understand that a considerable number of physicians in the Massachusetts Medical Society carry no insurance at all, some are apparently content to be defended by the Society and pay the cost of settlements, or judgments awarded by the court or jury, themselves. Others, chiefly graduates of unapproved medical schools, cannot obtain such insurance.

The premiums charged by those companies from whom we have been able to get figures are not uniform. It was stated that their premium rate is based on their experience in the Commonwealth. For example, for the same type of insurance for which the Medical Protective Company charges \$19 in Massachusetts, this same company charges \$16 in Pennsylvania. A company starting to underwrite malpractice insurance in a new territory may feel they can begin with a lower rate than charged by companies doing business for some time. But whether they can maintain such a rate will depend on their subsequent experience.

The Hartford Accident and Indemnity Company suggested the establishment of a committee within the Society to advise both the doctor, against whom a claim has been made, and the representative of the insurance company. This committee would study all claims or possible claims and advise both physician and insurance company as to the method to be pursued. According to their representative, New Hampshire has such a committee and has been able in seven years to reduce the cost of insurance for a surgeon with \$5,000/15,000 limits from \$60 to \$30 a year. The Medical Defense Committee of our society is consulted only by physicians carrying no malpractice insurance. Incidentally, should a plan similar to the New Hampshire one be adopted, the Hartford Accident and Indemnity Company will be glad to write policies subject to limits of \$10,000/30,000 at annual premiums of \$25 for general practitioners (exclusive of major surgery), \$32 for surgeons, and \$74 for x-ray specialists. This company will not differentiate as regards school but every applicant is checked by a credit bureau.

The American Policyholders' Insurance Company submitted a plan.

All members of good standing in the Society would be eligible.

No minimum or maximum number of members would be required.

The rates at the beginning would be as follows:

LIMIT	GROSS RATE	NET RATE (15% dividend)
\$10,000/30,000	\$20	\$17.00
15,000/45,000	22	18.70
20,000/60,000	24	20.40
25,000/75,000	26	22.10
50,000/150,000	28	23.80
100,000/300,000	30	25.50

These rates would be applied to all physicians and surgeons except those giving x-ray therapy, in which case the rates would increase 50 per cent. The above quoted rates are subject to a dividend of 15 per cent, which the company has paid to policyholders with this type of insurance uninterruptedly since its inception.

The procedure which they would employ is to be based on an agreement with the Society covering all features of the plan and individual policies are to be issued to each subscribing member. They will group the experience from time to time of the individual members as one unit and use the experience as the basis for rate adjustments. No physician other than a member of the Society would be eligible for insurance in this unit. After a period of twenty to twenty-two months, they expect to be able to judge their experience and will make revisions accordingly. The representative of the company feels that under this method of operation the members of the Society "could look forward with optimism to reduced rates from time to time while this plan is in operation." The company states they have been insuring physicians, dentists, and hospitals for many years and that they have written many county societies and specialist societies as groups. They are presently negotiating with some twenty-four medical societies.

The Lumbermen's Mutual Casualty Company, which has been writing malpractice insurance for over eight years in Massachusetts, submitted the following proposition

\$5,000/15,000 coverage to the general practitioner for \$25 the first year

A 20 per cent dividend would bring the second-year cost down to \$20

If one third of the membership of the Society is secured, they will give an additional \$5 discount, which will make the net cost \$15 per year

This applies to general practitioners only No figures were furnished as to surgeons and radiologists

The Medical Protective Company has reduced its limits to \$5,000/15,000 They state that the larger limits carried by physicians made the malpractice situation worse They feel that it increases the activity of the damage-suit lawyers and that this interest will lessen with smaller insurance targets, that it centers the attention of courts and juries on the question of insurance rather than on the issues in the trial, that it creates fictitious estates far beyond the actual means of the professional men carrying them, that it serves to invite large verdicts when there was no occasion for them, that it handicaps, or makes impossible, any reasonable compromises in difficult situations where such compromises are desired by the assured, that it increases rather than decreases the actual protection of a doctor and creates insurance for the damage-seeking plaintiff To follow this line of thought still further, it may be argued that any indemnity insurance may encourage the bringing of actions The plaintiff and his attorney may feel that any suit, if an insurance company is back of a physician, has a nuisance value. Relatively few suits against physicians when defended by a state medical society have been won in court

The Medical Protective rates are as follows

TYPE OF PRACTICE	LIMIT	RATE
Restricted surgery	\$2,500/ 7,500	\$19
Restricted surgery	\$5,000/15,000	22
Unrestricted surgery	2,500/ 7,500	25
Unrestricted surgery	5,000/15,000	30

Companies writing malpractice insurance in Massachusetts have to file an annual report at the State House Since all companies except the Medical Protective handle various types of insurance and "lump" their figures, only the Medical Protective figures are presented, as follows

RATE	INCOME	DISB	NET PREMIUMS WRITTEN	NET LOSSES	TOTAL ASSETS	SURPLUS TO POLICY HOLDERS	PER- CENT- AGE LOSSES IN SUITS TO PREMIUMS EARNED
1945	\$794,494	\$702,603	\$717,747 *46,850	\$133,178 *11,405	\$2,767,886	\$832,333	30.30
1944	726,369	674,047	647,809 *41,641	157,356 *13,117	2,675,482	787,607	15.84
1943	(Figures not available as statement is in hands of binder)						
1942	814,449	739,353	737,267 *48,701	242,123 *10,720	2,596,210	689,663	29.58
1941	921,095	1,283,343	829,343 *57,407	344,546 *15,750	2,520,434	663,725	31.69
1940	987,730	1,114,908	894,525 *62,785	417,167 *24,317	2,883,700	928,569	35.67

*These figures indicate Massachusetts business

The United States Fidelity and Guaranty Company begins coverage from \$10,000/30,000 Their rates vary according to specialty, ranging from \$19 to \$70, and they state that 40 per cent of their clients in Massachusetts qualify for the basic rate of \$19 This company has agreed to a 5 per cent decrease for all specialists, except x-ray This company is carrying hundreds of policies written in excess of \$10,000/30,000 A great many carry \$50,000/150,000 and some are \$100,000/800,000 This company entertains applications from graduates of unapproved schools who hold membership in the Society

In evaluating the relative merits of companies writing malpractice insurance, factors other than their financial stability and rates must be considered The experience and ability of their legal counsel are important, since malpractice suits are a highly specialized type of legal work Experienced agents may possibly also be of value It must not be overlooked,

however, that these agents usually work on a commission and that this commission is added to the cost of the premium

In view of the record of successful defense of suits by state medical societies, the advisability of the Massachusetts Medical Society undertaking its own indemnity insurance deserves consideration This idea is not new, it was mentioned by Dr Arthur W Allen in his report of the Committee on Medical Defense to the Council on February 6, 1946, and by Dr Walter P Bowers at a Council meeting twenty-five years ago

This report is submitted as one of progress Much more fact finding and study is necessary before recommendations can be made

CARL BEARSE, Chairman

* * *

The committee submitted a supplementary report giving data on the Mutual Protective Company for the years 1930-1940 (Table 1)

TABLE 1 Data on the Medical Protective Company (1930-1940)

YEAR	TOTAL INCOME	TOTAL DISBURSE- MENTS	MAS- SACHU- SETTS PREMI- UMS WRIT- TEN	MAS- SACHU- SETTS LOSSES PAID	TOTAL ADMITTED ASSETS	SURPLUS	PER- CENT- AGE OF LOSSES IN- CURRED TO PRE- MIUMS EARNED
1930	\$1,543,500	\$1,398,938	\$69,236	\$47,600	\$3,396,679	\$1,214,054	55.74
1931	1,451,930	1,494,559	72,993	33,503	3,365,448	1,198,826	64.22
1932	1,361,513	1,345,901	72,214	46,205	3,345,652	1,168,144	64.07
1933	1,128,752	1,362,079	69,391	56,351	3,137,442	1,003,777	56.50
1934	1,094,507	1,353,460	66,837	52,140	2,874,778	1,072,585	61.63
1935	1,172,012	1,147,795	71,562	52,453	2,898,629	1,017,241	52.71
1936	1,187,099	1,232,005	71,150*	65,105*	2,803,067	1,011,760	52.33
1937	1,216,428	1,075,828	71,291	35,711	2,946,715	1,017,132	56.64
1938	1,155,163	1,195,981	72,762	39,959	2,903,328	914,009	52.95
1939	1,037,095	983,384	67,038	31,613	3,007,819	925,988	54.87
1940	987,730	1,114,903	62,785	24,317	2,883,700	928,569	35.67

*This and the later figures are net those preceding are gross

APPENDIX NO 5

PROGRESS REPORT OF THE COMMITTEE TO MEET WITH GENERAL HAWLEY WITH VIEW OF FORMULATING PROGRAM IN MASSACHUSETTS FOR MEDICAL CARE OF VETERANS AND THEIR DEPENDENTS

The fee schedule approved by the Council of the Massachusetts Medical Society on April 10, 1946, was forwarded to the Veterans Administration in Washington

Word has been received from the Administration which alters only the form that this schedule should take No criticism of the fees submitted was offered

This communication indicated that a fee schedule should be submitted on two forms one to cover outpatient service and the other to cover service to veterans while confined to their homes or to hospitals The form covering the former service accompanied this communication It is herein reproduced

Fee Schedule for Outpatient Service

Submitted to Veterans Administration By

CLINICAL LABORATORY TESTS

- (1) Total and differential blood count including colorimetric hemoglobin estimation
- (2) Blood smear for malaria
- (3) Urinalysis, routine chemical and microscopic
- (4) Blood Wassermann (complement-fixation)
- (5) Blood Kahn (precipitation)
- (6) Spinal-fluid Wassermann (complement-fixation)
- (7) Spinal-fluid Kahn (precipitation)
- (8) Chemical examination of blood complete, including creatinine urea dextrose, nitrogen (or NPN) and uric acid
- (9) Sputum examination for tuberculosis (plain smear)
- (10) Determination of basal metabolic rate

SERVICES BY NONSPECIALISTS

- (11) Examination to determine need of hospitalization
- (12) Complete general routine physical examination
- (13) Office visit with treatment
- (14) Day visit to home or hospital (within city limits)
- (15) Night visit to home or hospital (9-00 p.m.-7-00 a.m.) (within city limits)
- (16) Charge for mileage one way for day or night visit outside city limits in addition to appropriate fee

EXAMINATIONS BY SPECIALISTS

- (17) General surgical
- (18) Orthopedic
- (19) Physical examination of heart
- (20) Complete examination of heart, including electrocardiogram
- (21) Electrocardiogram with interpretation
- (22) Physical examination of lungs
- (23) X-ray of lungs, flat plate
- (24) X-ray of lungs, stereoscopic
- (25) Gastrointestinal, including barium meal, x-ray and fluoroscopy
- (26) Dermatological
- (27) Allergy investigation (protein sensitization tests) including complete examination and report
For each 25 tests
- (28) Genitourinary examination without cystoscopy
- (29) Gynecological
- (30) Proctological
- (31) Psychiatric examination, complete
- (32) Neurological examination, complete
- (33) Examination of ears, nose and throat
- (34) Special ear examination, including audiometric test with chart
- (35) Special ear examination, including caloric or Barany test with report
- (36) Examination of eyes (to include either a copy of the prescription ordered or the retinoscopic correction of the refractive error, the fundus and field findings—the latter by chart in all cases of optic atrophy)
- (37) Examination of eyes with refraction if mydriatic is used (to include either a copy of the prescription ordered or the retinoscopic correction of the refractive error the fundus and field findings—the latter by chart in all cases of optic atrophy)
- (38) Examination by internist to determine diagnosis

TREATMENT BY SPECIALISTS

- (39) Dermatological first visit
- (40) Dermatological each subsequent visit
- (41) Ear, nose and throat first visit
- (42) Ear, nose and throat each subsequent visit
- (43) Ophthalmological first visit
- (44) Ophthalmological each subsequent visit
- (45) Psychiatric treatment (psycho-therapeutic conference), session of at least 50 minutes
- (46) Psychiatric treatment (psycho-therapeutic conference), session of 25 minutes or less
- (47) Neurological treatment (treatment is understood to be the usual follow-up care and observation after diagnosis has been made at original neurological examination)
- (48) Intravenous sodium amylal procedure

STANDARDS FOR NEUROPSYCHIATRISTS TO BE DESIGNATED FOR THERAPY PSYCHIATRISTS

Qualifications

- a Certified in psychiatry by American Board of Psychiatry and Neurology, or
- b Possession of one of following ranks in an accredited medical school
 - 1 Any professional rank in psychiatry
 - 2 Associate in psychiatry
- c Experience
 - 1 At least four years of two half days a week in an accredited mental hygiene clinic or similar institution in which modern therapeutic principles and techniques were practiced, or
 - 2 Certification by the American Psychoanalytical Association and four years practice of psychiatry using this, or other forms of modern psychiatric treatment or
 - 3 Two years' certified training and experience in the armed forces or in any other accredited institution in which intensive individual therapy was practiced and taught, with two additional years of similar practice, either private or institutional

NEUROLOGISTS

Qualifications

- a Certification in Neurology by American Board of Psychiatry and Neurology

We were informed by the Veterans Administration that the form which had to do with service rendered to veterans while confined to their homes and hospitals would be received later

The committee calls attention to the fact that the completion of the form submitted and herein reproduced makes it mandatory that the Society distinguish between the specialist and the nonspecialist, except in regard to psychiatrists and neurologists, in which instances the Veterans Administration itself sets the qualifications

The committee is very much aware of the difficulties which attend such a differentiation. It is its opinion that such differentiation is not within the scope of its authorization. It therefore finds it necessary to submit three questions to the Council. Shall such a differentiation be made? How shall it be arrived at? What formula shall be used whereby the fees paid to the specialist shall be differentiated from those paid to the general practitioner?

The committee has given much thought to this difficult subject. For the purposes of facilitating the discussion attending it, it submits two ideas with regard to the second question, provided the first question is answered in the affirmative. These are as follows

A suitable questionnaire be submitted to each member of the Society asking him to designate into which one of these two groups he believes he should be placed. (This method has been pursued by the Medical Service Administration of New Jersey)

To designate as specialists all those so certified by the specialty boards, those physicians who state that they limit their practice to a special field or who practice a specialty in an approved hospital as a member of that hospital's regular staff

With regard to the third question, again for the purposes only of facilitating discussion, the committee submits the following idea

That the schedule of fees approved by the Council on April 10, 1946, be regarded as specialists' fees and that, when the services called for in this schedule are rendered by general practitioners, the compensation shall be 20 per cent less than that set forth in that schedule. If the Council should adopt some such formula as this, it is necessary that the committee be allowed a leeway, not to exceed 5 per cent, so that the fees finally set down for the general practitioner shall appear in round numbers

The committee, in its report to the Council on April 20, 1946, recommended that the Blue Shield be the administrative agency in Massachusetts for the plan which concerned itself with the medical care by the civilian doctor of those for whom the Veterans Administration is responsible. The Council will remember that this type of administration was contrasted with that adopted by the Kansas State Medical Society. Under the latter plan, the Veterans Administration was its own administrative agent, the Society limiting itself to supplying the agency with a list of physicians willing to serve under schedule of fees agreed on and to maintain a close liaison with the Veterans Administration whereby the Administration would have the assistance of the Society in matters of dispute

The Council adopted this recommendation made by the committee. The committee now recommends that this action of the Council be rescinded

The committee is impelled to make this recommendation because of a distressing experience which the New Jersey Medical Service Corporation has had with an administrative plan similar to that approved by the Council on April 10, 1946

In the event that the Council adopts this recommendation, the committee will recommend the approval of the Kansas Plan modified so as to provide that the Blue Shield shall act as the liaison between the Veterans Administration and the physicians rendering the service in Massachusetts

In arriving at this latter recommendation the committee wishes to say that it has had only informal conversations with the Blue Shield on this subject.

The committee points out that until decisions are made with regard to these matters, its activities are at a standstill

HUMPHREY L. MCCARTHY, Chairman
JAMES K. BRAGGER
MICHAEL A. TIGHE

APPENDIX NO 6

REPORT OF THE COMMITTEE TO STUDY REVISION OF THE SALARIES OF THE EMPLOYEES OF THE SOCIETY

On May 21, 1946, a resolution was passed by the Council authorizing the President to appoint a special committee of three to study the matter of revision of the salaries of the employees of the Society and confer with the Committee on Finance. This committee was appointed and consists of Drs. Buck, Nye and Kickham

Your committee met and has given careful consideration to the subject matter as contained in the resolution. It was noted that there were three salaried employees and two officers of the Society who were compensated directly by the Society. Your committee in studying the matter weighed the fact that the employees of the Society are not beneficiaries under the Social Security Act and are not covered by any pension plan

Your committee is unanimous in the opinion that because of the increased cost of living, as indicated by all indices available, the compensation of the salaried employees of the Society who have been employed six months or more should

be increased by 20 per cent, retroactive to July 1, 1946 in the case of one employee who only recently joined the staff it is recommended to the proper committee that her salary be increased 20 per cent on January 1, 1947

Your committee also gave consideration to the compensation received by the two elected officers, namely, the Secretary and the Treasurer, whose compensation is paid by the Society. It is well recognized that the business and responsibilities of the Secretary have increased manifold in the last few years, and the same condition also prevails in the office of the Treasurer. In view of these facts, it is the considered opinion and recommendation of your committee that the compensation of the Secretary be increased from \$3,000 to \$4,000 per annum, and the compensation of the Treasurer be increased from \$2,000 to \$2,500 per annum, with increases retroactive to July 1, 1946

Your committee recommends that an extraordinary appropriation be made to cover this increased compensation for the period from July 1 to December 31, 1946, in the amount of \$1,332. The details of the recommended increases in compensation are as follows:

POSITION	PRESENT YEARLY COMPENSATION	RECOMMENDED YEARLY COMPENSATION	INCREASE IN 1946
Treasurer	\$2,000	\$2,500	\$250
Secretary	3,000	4,000	900
Executive Secretary	4,000	4,000	400
Miss Gaston	1,820	2,184	182
			\$1,332

These recommendations have been presented to the Committee on Finance, and have been approved by said committee.

CHARLES J KIRKHAM, Chairman
ROBERT W BUCK
ROBERT N NYE

APPENDIX NO 7

REPORT OF THE MASSACHUSETTS REPRESENTATIVES TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION JULY 1-5, 1946

I present this report as the senior member of your delegation attending the meeting of the House of Delegates in San Francisco from July 1 to 5, 1946. There was a full attendance, despite the distance and difficult travel conditions.

This marked the first time that the newly authorized Section on General Practice had its delegate sit in on the deliberations. In the assignment of the various reference committees your representatives fared well — Walter Phippen to the important Committee on Miscellaneous Business, Dwight O'Hara to Sections and Section Work, Leland McKinnick to Medical Education, and others of us to other committees. As I stated in my report of last December, we cannot give too much praise and appreciation to the tremendous amount of earnest and intelligent work performed by these reference committees. They are the works or machinery, and make possible the really large amount of work done. The addresses of President Lee, President-Elect Shuldene, and Speaker Fouts were all earnest, thoughtful and convincing, and on the usual high plane. These are all well worth reading and appear in the July 13 issue of the *Journal of the American Medical Association* (pages 905, 907 and 908).

The balloting for the Distinguished Service Award resulted in an overwhelming vote for the eminent physiologist from Chicago, A. J. Carlson, at the meeting held later on Tuesday evening he was given this award *in absentia*.

At this point one may mention Speaker Fouts, serving for the first time, he having been elected only last December at Chicago. He proved himself as able, efficient and eminently fair presiding officer. Speakers usually serve until they choose to resign, and this commonly is a matter of six or seven years (or more). He deserved re-election. California, however, had other ideas and proposed Dr. Goin, of Los Angeles, a most able man. The balloting resulted in the re-election of Fouts by the narrow margin of 90 to 77. California did not move to make it unanimous.

The usual long reports of the officers (Secretary, Treasurer and various councils) reading of the hills and report from the Washington office of the American Medical

Association, and the report of the Committee on Postwar Planning, filled up the morning of the first day. The details of all these reports should be read in the journals of July 6 and 20. They are much too long and detailed to lend themselves to easy summary. Also worth reading is the editorial on page 974 of the July 20 number.

On the afternoon of the first day, there were further long committee reports dealing particularly with rural medical service in the Middle West, Far West and South — the great open spaces. The usual amount of new business was offered and was referred to the various reference committees.

On the morning and afternoon of the second day, reports of the various reference committees were presented to be acted on then, or debated and referred back, a not uncommon procedure.

To show how deeply involved the American Medical Association is in industrial matters one should read the report of the Committee on Executive Session, with reference to the national bituminous wage agreements (pages 993, 994, 995 and 996 in the July 20 number of the *Journal of the American Medical Association*), which are of most vital importance in some parts of the country.

Wednesday, July 3, was an open date for the delegates except for the members of the various reference committees, there was no holiday for them. There was also no meeting of the delegates on Thursday morning.

On the afternoon of Thursday (the final day) all reference committees' reports, for the most part fairly long, were acted on, usually without much debate. Then came the reports of the chairman of the Board of Trustees, Dr. Sensenich, on the changes in organization of the American Medical Association in accordance with the recommendations of the Rich Public-Relations Report. This report had but just been received and was so long it could only be sketchily summarized. The following is essentially what transpired:

Changes in the organization of the American Medical Association in accord with the recommendations of the Rich Public Relations Report were approved by the House of Delegates.

The Bureau of Medical Economics is to be expanded with a leading economist employed to develop factual material in the field for use in the *Journal of the American Medical Association and Hygiene*.

The general manager is to have an executive assistant — an expert in the field of public relations — to interpret the activities of the various councils and bureaus to the public and medical profession.

The name of the Council on Medical Service and Public Relations was changed to the Council on Medical Service.

Although the title of the Council was shortened its field of operation and duties was enlarged. The Division of Prepayment Plans has definitely been placed under it, putting the Ten Point Program into actual practice is one of its major concerns. It will intensify its work in the field of professional relations extending the scope of the regional conferences and the "News Letters." The House of Delegates instructed it to develop the health-council idea and approved its recommendation for the creation of a speakers' bureau. The Washington office of the Council remains intact.

It was agreed that a special committee, not a reference committee, should be appointed to study, with the Trustees this Rich report before the next session of the House of Delegates and bring to its recommendations. I particularly call to your attention the minutes of the third meeting on Thursday afternoon (page 999 *et seq.*) dealing with legislation and public relations.

The election of officers concluded the meeting. Olin West for nearly twenty-five years the most efficient secretary of the American Medical Association, was unanimously elected president-elect. The affection and respect for this man among the delegates is difficult to express. He is most worthy of it. His remarks after the election are found on page 1004 of the July 20 number. These remarks were made entirely offhand, without notes, and clearly characterize the man and his ideals. They should be read.

The following are a few incidentals:

Hereafter there are to be two sessions a year of the House of Delegates, the mid-winter meeting to be held in Chicago.

The next meeting in 1947 (Centennial) is to be held in Atlantic City, 1948 in St. Louis, 1949 in New York City (provided the rates for the hiring of halls are not prohibitive)

A rising vote was called for on the Wagner-Murray-Dingell bill, it was unanimous. I observed no one sitting.

California and the San Francisco County Medical Society well deserve the hearty congratulations of the American Medical Association for their remarkable efficiency and open-handed generosity.

It was a good meeting, free from the element of pressure so noticeable last December at Chicago. It was felt certain that Congress would not act on the health bills this term, thereby giving the various voluntary prepayment methods a chance to get well under way.

DAVID D. SCANNELL

APPENDIX NO 8

COMMUNICATION

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street, Chicago 10

August 9, 1946

Dr. Michael A. Tighe, Secretary
Massachusetts Medical Society
Boston, Massachusetts

Dear Dr. Tighe:

At the recent meeting of the House of Delegates of the American Medical Association in San Francisco, a proposed amendment to the by-laws was submitted by Dr. James C. Sargent, Wisconsin. This was referred to the Reference Committee on Amendments to the Constitution and By-Laws. Dr. Lowell S. Goin, California, chairman. The Reference Committee in its report on the proposed amendment recommended that it be not adopted and suggested instead the adoption of the following resolutions. The report of the Reference Committee, including the resolutions, was adopted. The resolutions are as follows:

RESOLVED, That it is a policy of the House of Delegates that resolutions should be introduced at least thirty days prior to any meeting of the House and be it further

RESOLVED, That such resolutions be published in the *Journal* and in the "Handbook of the House of Delegates," and be it further

RESOLVED, That the secretary of the Association be directed to write annually to the secretary of each constituent association requesting that all resolutions adopted by the said constituent association and requiring the attention of the House of Delegates of the American Medical Association be submitted to the secretary's

office as far in advance of the meeting of the House of Delegates as may be possible, and that the secretary request that the communication be read in the House of Delegates of each constituent association, and be it further

RESOLVED, That the secretary be directed and authorized to secure sufficient assistance to mimeograph all resolutions submitted in compliance with this request so that each delegate may have in his possession at the opening of the House of Delegates copies of the resolutions to be introduced at that time.

This is being brought to your attention as a result of the adoption of the resolution.

Very sincerely yours,

[Signed] GEORGE F. LULL, M.D.

GEORGE F. LULL, M.D.

Secretary and General Manager

APPENDIX NO 9

COMMUNICATION

FEDERAL SECURITY AGENCY

PROCUREMENT AND ASSIGNMENT SERVICE

Washington, June 10, 1946

Dr. Michael A. Tighe, Secretary
Massachusetts Medical Society
8 The Fenway, Boston, Massachusetts

Dear Dr. Tighe:

For practical purposes the functions of the Procurement and Assignment Service have been terminated and the activities of the several state offices brought to a close. The success of the program in meeting the needs of the armed forces without sacrificing the civilian population may be attributed directly to the patient and tireless devotion of many state committees and countless local advisers. Many of these committeemen and advisers are unknown to the Directing Board, except through the results of their efforts, and it would obviously not be practicable to undertake to communicate with them.

In a recent letter to each state chairman, I asked that the appreciation of the Directing Board be conveyed to all the state and local representatives whose full co-operation was essential to the ultimate achievement. The Directing Board at its final meeting on May 17, 1946, resolved that the untiring efforts, kind tolerance and successful accomplishment of these state committee members and local advisers be commended to the appropriate professional state society for suitable recognition by the society.

I hope you will draw this recommendation to the attention of your society, and that it will be disposed to afford some such recognition.

Sincerely yours,

[Signed] FRANK H. LARBY, M.D.

FRANK H. LARBY, M.D.

Chairman, Directing Board

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

CASE 32501

PRESENTATION OF CASE

First admission A sixty-seven-year-old housewife entered the hospital because of a lesion on the left side of the tongue. Except for a blood pressure of 190 systolic, 110 diastolic, physical examination and routine blood studies were negative. The urine had a specific gravity of 1.004 and 1.007 and contained few to many white cells per high-power field; there was a ++ test for albumin and no sugar. An epidermoid carcinoma (Grade II) of the tongue was resected, and the patient was discharged on the tenth postoperative day.

Final admission (eight months later) After operation the patient was examined regularly in the Tumor Clinic. A month before admission lymph nodes were palpated in the submaxillary regions and in the left side of the neck. The patient had no other complaints. There was no history of systemic disease other than hypertension.

Physical examination disclosed a palpable lymph node in the floor of the mouth. Beneath the left sternomastoid muscle lay a movable hard mass measuring 3.5 x 2.5 cm. A loud systolic murmur was audible in the mitral area.

The temperature was 98.6°F, the pulse 80, and the respirations 18. The blood pressure was 220 systolic, 130 diastolic.

Examination of the blood showed a hemoglobin of 11 gm per 100 cc and a white-cell count of 8000. The specific gravity of the urine was usually below 1.010, but registered 1.020 on one occasion. Tests for albumin ranged from 0 to ++++. On admission the sugar reaction was orange. Many white cells per high-power field, often in clumps, were usually seen in the sediment. The fasting blood sugar was 286 mg and the nonprotein nitrogen 70 mg per 100 cc. In the x-ray films the heart was of normal size. An area of increased density extending from the left lateral chest wall had somewhat the appearance of an old infarct. An electrocardiogram was interpreted as representing left ventricular hypertrophy and strain.

During the preoperative course insulin was given. The blood sugar never fell below 220 mg per 100 cc,

but the urine tests remained green after the third day. With the administration of large amounts of fluid the nonprotein nitrogen stabilized between 60 and 70 mg per 100 cc. The cholesterol was 284 mg per 100 cc, and the chloride 98 milliequiv and the carbon dioxide 26 milliequiv per liter. A callus on the right foot infected with beta-hemolytic streptococci caused considerable local swelling for several days and was accompanied by a daily temperature of 100 to 101°F. From the eighth to the seventeenth day, 192,000 units of penicillin were given, and the drug was then discontinued. The temperature was normal from the fourteenth to the twentieth hospital day, when a radical dissection of the left side of the neck was carried out, with removal of several carcinomatous lymph nodes. On the following day the temperature rose to 102°F, the pulse and respirations were rapid. The blood sugar was 500 mg per 100 cc and ranged from 360 to 600 mg thereafter, despite dietary treatment and insulin. There were moist rales at both lung bases.

During the week following operation the temperature gradually fell to 100°F. The wound progressed satisfactorily, and the stitches were taken out on the twenty-eighth hospital day. There was a pocket of pus in its upper angle, from which a moderate number of colon bacilli and many colonies of *Staphylococcus aureus* were obtained on culture. Meanwhile, the nonprotein nitrogen had risen to 115 mg per 100 cc, and the chloride and carbon dioxide had fallen to 90 and 21 milliequiv per liter respectively. The patient was semistuporous, with fast, shallow respirations. A chest x-ray film was negative on the third postoperative day. By the tenth postoperative day the patient was in deep coma. Respirations were fast, shallow and gasping, and the nonprotein nitrogen had risen to 170 mg per 100 cc. Death occurred on the same day.

DIFFERENTIAL DIAGNOSIS

DR. WILLIAM BECKMAN: It is evident from the record that the patient had at least three diseases that are potentially fatal: carcinoma, diabetes and nephritis. The problem seems rather to decide which of these was the most important and what the relation was between any or all of them. We do not have any trouble making the diagnosis of carcinoma of the tongue because we are kindly told that it was present — there was pathologic evidence in both tongue and lymph nodes. I do not believe that carcinoma of the tongue is apt to metastasize far away from the local site, and I therefore doubt that metastasis was closely connected with this patient's death.

Either one or both of the other conditions mentioned are likelier causes. We can make a diagnosis of diabetes because we have the usual criteria for that diagnosis: a high fasting blood sugar, accompanied by sugar in the urine. By and large, when one thinks of diabetes one thinks of a condition

that is occasioned by an inadequate supply of insulin. The body cannot make enough insulin to supply its needs, but a high blood sugar and glycosuria occur in other conditions not due to insulin lack, such as obesity with diabetes, which clears up when the patient reduces, and intercapillary glomerulosclerosis, which is a special pathologic entity, with diabetes as an associated symptom. It is also an associated symptom in other conditions, such as Cushing's disease, in which it is not affected by the administration of insulin so much as it is in diseases in which insulin lack is the primary disturbance. I think that this diabetes fell into the type not affected by insulin, because the patient was given a great deal of it, although we do not know how much, but the blood sugar was never brought below 200 mg per 100 cc which is about twice normal according to our laboratory.

We are also able to make the definite diagnosis of nephritis of some sort. The patient had high blood pressure, albuminuria and an elevated nonprotein nitrogen in the serum. Those three things are sufficient to make the diagnosis of nephritis, although they do not help much in deciding the type. Apparently, there was pus in the urine, which suggests pyelonephritis. I think that this is the most frequent kind of nephritis in a patient of this age, although vascular nephritis is certainly a close second. There is little to suggest primary glomerulonephritis. In any event, the patient had severe chronic nephritis. She had a severe infection during the hospital stay, and it is well known that infection accentuates both diabetes and nephritis. The final episode was one of coma, which occurs both in diabetes and in the terminal stages of nephritis, so that it is important to differentiate them. It is quite improbable that the patient had diabetic acidosis because she did not have acetonuria and because the carbon dioxide content of the blood, although slightly reduced, was only 21 milliequiv per liter, which is the lower limit of normal and well out of the range of diabetic acidosis. I am therefore forced to the conclusion that the terminal episode was coma due to renal failure rather than to diabetes, this is further indicated by the marked rise in nonprotein nitrogen that occurred terminally. In such a situation, it is tempting to relate the two conditions, diabetes and nephritis, in terms of intercapillary glomerulosclerosis, but I do not see how that is possible on the basis of the information that is given. I hold to the principle that one cannot make the diagnosis of intercapillary glomerulosclerosis unless there are definite changes in the optical fundi—I used to believe that this was always true, but I was wrong. In one of these exercises, Dr Earle Chapman* discussed a case—without preparation, by the way—and correctly made the diagnosis of intercapillary glomerulo-

sclerosis on the basis of the association of diabetes and nephritis, in spite of the fact that the patient, whom I had taken care of during life, had normal fundi up to the time of death.

My diagnoses are cancer of the tongue, which presumably was not related to the terminal episode, diabetes, which did not produce the final coma, and chronic nephritis—presumably chronic pyelonephritis. I do not believe that I have enough evidence to make a diagnosis of intercapillary glomerulosclerosis.

DR REED HARWOOD: Was this patient given large doses of insulin?

DR BEVERLY TOWERY: Large doses were not given because the patient seemed to have a high penetration level for sugar. The dose was fairly low. The attempt was not made to get the blood sugar down much below 200 mg per 100 cc.

DR HARWOOD: After the operation did the blood sugar remain between 360 and 500 mg per 100 cc?

DR TOWERY: Yes. It brought up the question in our minds whether the patient had acute disease in the pancreas following operation as a result of which the insulin supply had been suddenly reduced. Whether that is true or not I do not know. On the day before death she received a total of about 60 units of insulin in divided doses.

DR HARWOOD: That is not a large dose for a person running such a high blood sugar.

CLINICAL DIAGNOSES

Uremia
Nephrosclerosis
Pyelonephritis
Diabetes
Hypertension
Arteriosclerotic heart disease

DR BECKMAN'S DIAGNOSES

Cancer of tongue, with local metastases
Chronic pyelonephritis, with uremia
Diabetes mellitus

ANATOMICAL DIAGNOSES

Acute coronary thrombosis, with cardiac infarction
Nephrosclerosis
Subacute pancreatitis, with fat necrosis
Chronic cholecystitis and cholelithiasis

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY: This patient was quite a museum of pathologic findings at autopsy. Dr Beckman was correct in his prediction that the carcinoma of the tongue had nothing directly to do with her death. There were only regional metastases in the cervical lymph nodes. There was no extensive carcinomatosis. The kidneys, which were rather small and contracted, showed on microscopic examination a severe grade of arteriosclerosis. I think that the involvement was advanced enough to make it quite reasonable to assume that the

*Case Records of the Massachusetts General Hospital (Case 30351).
New Eng J Med 231:333-337, 1944

patient died in uremia. There was another factor, however, that probably contributed to death and perhaps also to the renal insufficiency. There was a very large area of fresh infarction in the myocardium, with a thrombus of corresponding age in the left descending coronary artery. Sudden myocardial failure may have terminally increased the degree of renal failure.

The surprise of the autopsy was the pancreas. As soon as the abdomen was opened and the omentum reflected, it was noted that the undersurface of the omentum was dotted with yellowish cheesy areas. The pancreas itself was greatly enlarged, weighing about 400 gm, and was filled with yellow, cheesy masses. Grossly, no normal pancreatic tissue could be recognized, and microscopically only the smallest islets persisted here and there. It is tempting to assume that the diabetes was directly due to destruction of the pancreas. That is a relatively rare event. We see a great many cases of pancreatitis in which there is massive destruction of pancreas and in which no diabetes develops. On the other hand, there was no sugar in the urine during this patient's first hospital stay only eight months before the second entry, when she was proved to be severely diabetic. I therefore think that the evidence in this case is fairly good that pancreatic necrosis was the direct cause of the diabetes. As so often in pancreatitis, there was chronic infection of the gall bladder and cholelithiasis.

DR. TOWERY: How acute was the process in the pancreas?

DR. MALLORY: It was essentially old. There was nothing whatever in the clinical history, of course, from start to finish, to suggest an attack of acute pancreatitis, except perhaps the blood sugar.

DR. EDWARD BENEDICT: What would have happened if she had been given massive doses of insulin? Would she have improved?

DR. MALLORY: I think that she died of uremia, complicated by cardiac failure, and that neither the diabetes nor the cancer of the tongue was in any way responsible for death.

DR. BECKMAN: Would you not rather say that it was cardiac failure complicated by uremia, because of the fact that the nonprotein nitrogen rose so rapidly as a result of the congestive failure?

DR. MALLORY: That is a better way to put it. The lungs were markedly congested and edematous.

hot and cold sensations. Pain developed and became so intense that the patient was completely incapacitated. The most recent menstrual period had started six days before admission and was almost at an end. The patient had had intercourse before the onset of the period. There had been no intermenstrual bleeding or discharge. Periods occurred every twenty-eight days, lasting about a week. There had been no frequency, urgency, hematuria or dysuria.

Five years before admission the patient had had a ruptured ectopic pregnancy. Ten years earlier the appendix had been removed.

Physical examination revealed a healed midline, suprapubic scar and a right paramedian scar. The abdomen was soft, with tenderness above the pubis. There were no masses. Blood was trickling from the cervical canal. There was a feeling of fullness in the right vault. Motion of the cervix caused severe pain. Rectal examination was negative except for pain on motion of the cervix.

The temperature was 100°F, and the blood pressure was 100 systolic, 60 diastolic.

Examination of the blood disclosed a red-cell count of 4,200,000, with a hemoglobin of 10.0 gm, and a white-cell count of 11,500. The urine was normal. No gram-negative cocci were seen on vaginal smear.

After the patient had been put to bed the pain rapidly improved and subsided completely. She felt better, but there was suprapubic tenderness. About two hours after admission a slight, constant lower abdominal pain began and was accompanied by slight spasm in the right lower quadrant. Three and a half hours after admission the pain was again severe, and a mass was felt by pelvic examination to the right of the uterus. The white-cell count had risen to 13,700, with 84 per cent neutrophils.

An operation was performed half an hour later.

DIFFERENTIAL DIAGNOSIS

DR. FRANCIS M INGERSOLL: It is apparent from the history that an acute surgical emergency existed. A frequent condition that accounts for this type of history and physical findings is an ectopic pregnancy, which is suggested by certain outstanding findings in this case. First of all, the patient had a history of a previous ectopic pregnancy, and it is well known that a person who has had one ectopic pregnancy is liable to have a second. The suddenness of the onset of symptoms is also in favor of the diagnosis. The course in the hospital is not typical but fits in with what happens after an ectopic pregnancy ruptures. The lesion starts to bleed, the rupture seals off, the bleeding stops and on pelvic examination little is found. I remember a patient with ectopic pregnancy in whom examination failed to reveal bleeding. I told her to call me if anything happened. When I got home I had a

CASE 32502

PRESENTATION OF CASE

A twenty-seven-year-old married tripara, a nightclub singer, entered the hospital complaining of severe, continuous lower abdominal pain.

Three hours before admission an uneasy feeling had begun in the lower abdomen accompanied by

that is occasioned by an inadequate supply of insulin. The body cannot make enough insulin to supply its needs, but a high blood sugar and glycosuria occur in other conditions not due to insulin lack, such as obesity with diabetes, which clears up when the patient reduces, and intercapillary glomerulosclerosis, which is a special pathologic entity, with diabetes as an associated symptom. It is also an associated symptom in other conditions, such as Cushing's disease, in which it is not affected by the administration of insulin so much as it is in diseases in which insulin lack is the primary disturbance. I think that this diabetes fell into the type not affected by insulin, because the patient was given a great deal of it, although we do not know how much, but the blood sugar was never brought below 200 mg per 100 cc which is about twice normal according to our laboratory.

We are also able to make the definite diagnosis of nephritis of some sort. The patient had high blood pressure, albuminuria and an elevated nonprotein nitrogen in the serum. Those three things are sufficient to make the diagnosis of nephritis, although they do not help much in deciding the type. Apparently, there was pus in the urine, which suggests pyelonephritis. I think that this is the most frequent kind of nephritis in a patient of this age, although vascular nephritis is certainly a close second. There is little to suggest primary glomerulonephritis. In any event, the patient had severe chronic nephritis. She had a severe infection during the hospital stay, and it is well known that infection accentuates both diabetes and nephritis. The final episode was one of coma, which occurs both in diabetes and in the terminal stages of nephritis, so that it is important to differentiate them. It is quite improbable that the patient had diabetic acidosis because she did not have acetonuria and because the carbon dioxide content of the blood, although slightly reduced, was only 21 milliequiv per liter, which is the lower limit of normal and well out of the range of diabetic acidosis. I am therefore forced to the conclusion that the terminal episode was coma due to renal failure rather than to diabetes, this is further indicated by the marked rise in nonprotein nitrogen that occurred terminally. In such a situation, it is tempting to relate the two conditions, diabetes and nephritis, in terms of intercapillary glomerulosclerosis, but I do not see how that is possible on the basis of the information that is given. I hold to the principle that one cannot make the diagnosis of intercapillary glomerulosclerosis unless there are definite changes in the optical fundi—I used to believe that this was always true, but I was wrong. In one of these exercises, Dr Earle Chapman* discussed a case—without preparation, by the way—and correctly made the diagnosis of intercapillary glomerulo-

sclerosis on the basis of the association of diabetes and nephritis, in spite of the fact that the patient, whom I had taken care of during life, had normal fundi up to the time of death.

My diagnoses are cancer of the tongue, which presumably was not related to the terminal episode, diabetes, which did not produce the final coma, and chronic nephritis—presumably chronic pyelonephritis. I do not believe that I have enough evidence to make a diagnosis of intercapillary glomerulosclerosis.

DR REED HARWOOD: Was this patient given large doses of insulin?

DR BEVERLY TOWERY: Large doses were not given because the patient seemed to have a high penetration level for sugar. The dose was fairly low. The attempt was not made to get the blood sugar down much below 200 mg per 100 cc.

DR HARWOOD: After the operation did the blood sugar remain between 360 and 500 mg per 100 cc.?

DR TOWERY: Yes. It brought up the question in our minds whether the patient had acute disease in the pancreas following operation as a result of which the insulin supply had been suddenly reduced. Whether that is true or not I do not know. On the day before death she received a total of about 60 units of insulin in divided doses.

DR HARWOOD: That is not a large dose for a person running such a high blood sugar.

CLINICAL DIAGNOSES

Uremia
Nephrosclerosis
Pyelonephritis
Diabetes
Hypertension
Arteriosclerotic heart disease

DR BECKMAN'S DIAGNOSES

Cancer of tongue, with local metastases
Chronic pyelonephritis, with uremia
Diabetes mellitus

ANATOMICAL DIAGNOSES

Acute coronary thrombosis, with cardiac infarction
Nephrosclerosis
Subacute pancreatitis, with fat necrosis
Chronic cholecystitis and cholelithiasis

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY: This patient was quite a museum of pathologic findings at autopsy. Dr Beckman was correct in his prediction that the carcinoma of the tongue had nothing directly to do with her death. There were only regional metastases in the cervical lymph nodes. There was no extensive carcinomatosis. The kidneys, which were rather small and contracted, showed on microscopic examination a severe grade of arteriosclerosis. I think that the involvement was advanced enough to make it quite reasonable to assume that the

*Case Records of the Massachusetts General Hospital (Case 30351)
New Eng J Med 231:333-337, 1944

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CONFUSION WORSE CONFOUNDED

THERE are some famous lines in *Paradise Lost*, describing the flight of Satan's band,

for such a numerous host
Fled not in silence through the frightened Deep,
With ruin upon ruin, rout on rout,
Confusion worse confounded,

that a year ago would have been considered particularly appropriate to the hosts, undoubtedly of evil, recently routed by the victorious United Nations, this year, although we are still certain of who was defeated, considerable doubt may be entertained regarding who is victor

Scarcely more than a year ago our own nation, despite some industrial unrest, was a unified, integrated machine set to produce a single result — the maintenance of national security against dangers from without. Each man was at work, but his labors were for a purpose: he could put his hand upon his neighbor's shoulder and call him comrade — they were working toward a common goal. "Sweet," wrote Shakespeare, "are the uses of adversity", we knew them then.

This year, frustration is in the atmosphere, we have no sun of York to shine on the winter of our discontent. Most of us are still hard at work, particularly the doctors of our acquaintance who meet no longer with a wartime forbearance on the part of a mutually striving clientele. But many are not working at all, a fumbling policy having put them on the dole, many veterans of all ages are unable again to become average citizens. Government control has broken down, and inflation is consuming reasonable profits. We are facing and failing to cope with materialism and moral disintegration within, and we are failing to accept world leadership without.

We are permitting the Great Patriot, the king of the coal fields, to hold his knife at the throats of a hundred and forty million Americans, mindless of the fact that the days of rugged individualism are over, and that no gain of great importance can be made by anyone without a co-operative effort on the part of those involved.

We are hard at work, — except for those who do not work at all, — but we are working without the solidarity that comes from working in a common cause. We have little patience with each other, we have lost our feeling of neighborliness. True, we share a common anxiety, but we are also victims of a common selfishness that will last until we again have a mutual goal to unite us in some constructive effort. That goal can consist of no material devices. Among ourselves and with the rest of the world, the most urgent issue on which to unite today is that of world peace. This is our desideratum. We shall not overcome our present insecurity until we can feel that we are striving, with other nations, for that end.

frantic telephone call saying that something had happened within ten minutes after I had left the patient's house. At operation she had a bleeding ectopic pregnancy. In the case, under discussion, the patient had first an indefinite and later a definite mass, probably due to further hemorrhage. Also, exquisite tenderness on motion of the cervix was noted on both vaginal and rectal examination. That is characteristic of an ectopic pregnancy. Motion of the cervix causes motion of the partially ruptured ectopic pregnancy, and pain is elicited. This sign is not confined to ectopic pregnancy, however, being found in twisted cyst of the ovary or pelvic inflammation.

The red-cell count was slightly low, but I do not believe that that is a help in the final diagnoses. If it had been markedly lowered, we should be more convinced that the patient was bleeding intraperitoneally. I do not believe that the patient had bled enough to lower the red-cell count markedly. The white-cell count is consistent with ectopic pregnancy.

A few facts are against the diagnosis of an ectopic pregnancy. First, the patient had not missed a period. We know, however, that patients can have perfectly normal periods with pregnancy in the tube or ovary. Secondly, the only intercourse mentioned was immediately prior to the onset of the last period, and this statement implies that there had been no other intercourse in recent weeks, so that she could not have been pregnant.

What other conditions are possible? Pelvic inflammation due to gonorrhea comes to mind. The acuteness of the onset of pain, the lack of spasm and the fact that no gonococci were found in the vagina make it unlikely that the patient had pelvic inflammation. A rare condition is torsion of a normal fallopian tube. Twisted ovarian cyst can give all the same symptoms and is a possibility in this case. Against it is the fact that no discrete mass was felt at the first examination. Another possibility is a ruptured ovarian cyst accounting for the severe pain and the physical findings described. That is unlikely, however, and in conclu-

sion I believe that this patient had an abdominal emergency that necessitated operation, and I believe that the most probable diagnosis is an ectopic pregnancy.

CLINICAL DIAGNOSIS

Twisted ovarian cyst?
Pelvic inflammatory disease?
Ectopic pregnancy?

DR INGERSOLL'S DIAGNOSIS

Ectopic pregnancy

ANATOMICAL DIAGNOSIS

Ectopic pregnancy

PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY. At operation a hemorrhagic mass was found at the fimbriated end of the right tube, the left tube and ovaries having been resected previously, as the history stated. There was approximately 300 cc of blood in the abdomen. The tube was removed, the histologic examination showed numerous chorionic villi distributed in decidual tissue, a characteristic finding of tubal pregnancy.

DR GEORGE CLOWES. A few points of interest are not brought out in the record. When the patient first came in, the mass described in the pelvis was not palpable. Both vaults were felt to be clear. Then, with the recurrence of pain, she was again examined, and a mass was thought to be felt by one examiner, although another observer was not able to confirm it.

DR BEVERLY TOWERY. Did she have hemorrhage into the broad ligament?

DR CLOWES. The blood was free in the peritoneal cavity, and there was no hemorrhage in the broad ligament.

DR HOWARD ULFELDER. What was the duration of the pregnancy?

DR MALLORY. I was trying to guess that. It could have been two weeks, although I am inclined to believe that it was longer than that.

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NECROTIZING RENAL PAPILLITIS A FORM OF ACUTE PYELONEPHRITIS

STANLEY L. ROBBINS, M.D.,* G. KENNETH MALLORY, M.D.,† and THOMAS D. KINNEY, M.D.‡

BOSTON

NECROSIS of the renal papillae, sometimes termed "papillitis necroticans"¹ or "necrotizing pyelonephritis,"² is an infrequently recognized and severe type of suppurative renal infection that is usually encountered in diabetic patients although it is occasionally found in nondiabetic persons.^{3, 4} The lesion, which has been a well recognized pathologic entity for many years, was recently well described by Günther.⁵ It remains, however, a poorly defined clinical entity that is usually found as an unexpected lesion at autopsy. Recent publications emphasize the fact that the problem of acute pyelonephritis—in particular that of necrotizing papillitis—is of greater magnitude than its obscurity indicates. In 1942 Harrison and Bailey² clearly demonstrated that infections of the urinary tract in diabetes are not only frequent but also usually asymptomatic of 50 diabetic patients studied, 27 had bacteria in the urine on a direct smear examination of the sediment and 10 showed completely unsuspected pyuria. In contrast, only 4 control patients out of 50 had bacteriuria, 2 of them had associated pyuria. These results suggest that latent infections of the urinary tract are extremely frequent in diabetic patients and in many cases may serve as foci for the development of the severer lesions under discussion. That these infections are not merely potential hazards is borne out by the fact that 67 per cent of the diabetic patients on whom autopsies were performed at the Mallory Institute of Pathology from 1933 to 1942 died chiefly as a result of acute pyelonephritis.⁶ Significantly, most of this group had necrotizing papillitis.

During the years 1932 to 1945, post-mortem examination disclosed 26 cases of this lesion at the Mallory Institute of Pathology, Boston City Hospital, and at the Peter Bent Brigham Hospital, 19 of which occurred in diabetic and the remaining 7 in nondiabetic patients.

This paper presents a clinical and pathologic analysis of this series of diabetic and nondiabetic patients who at autopsy were found to have necrosis of the renal papillae. With continued study of anatomically verified cases, it is to be hoped that the clinical picture of this syndrome will become established as a clearly defined entity.

On review of the series of cases under discussion it at once became apparent that they tended to assume one of several clinicopathologic patterns that recurred with remarkable constancy throughout the series. The following representative cases have been selected for citation.

CASE 1. S. F. (B.C.H. 1,160,583), a 61-year-old woman, entered the hospital with the complaint of a red, tender, swollen left lower leg. She had stumbled against a chair 6 days before entry, injuring the leg, and since that time the discomfort and swelling had been steadily progressive despite local applications of heat. She was known to have had diabetes for "many years," which had apparently been controlled by a diet supplemented with 8 units of regular insulin daily. There was no history of previous infections or diabetic accidents.

Physical examination disclosed a well oriented patient in no obvious distress. The only finding of significance was the presence of a fluctuant, red area of marked tenderness over the lateral aspect of the distal left lower half of the leg.

Examination of the urine showed a trace of albumin, a green to orange Benedict reaction and a rare white cell per high-power field. The fasting blood sugar varied between 229 and 418 mg per 100 cc. The serum nonprotein nitrogen was 39 mg per 100 cc on admission.

The fluctuant area of the left lower leg was incised, and *Staphylococcus aureus* was cultured from the pus. Sulfadiazine and penicillin in full dosages were administered, and the temperature soon became normal and the incised wounds appeared to be slowly healing. The diabetes mellitus was well controlled with 20 units of regular insulin daily. After 2 weeks of apparent improvement, however, the temperature began to swing from 101 to 102°F. The urine contained innumerable white cells despite all medication, and the patient ran a severely septic febrile course terminating in stupor, coma and death during the 6th hospital week. A hemolytic *Staph. aureus* was cultured from the blood.

Autopsy. On gross examination the kidneys were enlarged, their combined weight was 300 gm. The capsular surfaces were free from cortical abscesses. On section several large, triangular areas including the entire tips of some of the papillae in each kidney were yellow green and completely necrotic. Several discrete abscesses, 0.2 to 0.3 cm in diameter, were present at the corticomedullary junction above these areas of papillary necrosis. The only other significant findings were a healing abscess over the left ankle.

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AN EYE FOR AN EYE

THE Massachusetts Eye and Ear Infirmary has laudably set up what is known as "The New England Eye Bank" which is affiliated with the Eye Bank for Sight Restoration, Incorporated, of New York City. In the minds of certain lay persons, however, there are two misconceptions regarding it. In the first place, there is the erroneous idea that *any* type of blindness can be cured by the substitution of a donor's eye. Secondly, it is rather widely believed that if an eye is not used within seventy-two hours it is completely wasted.

There is only one type of blindness that can be cured or improved in this manner, namely, that due to corneal opacities. Of the approximately 250,000 blind persons in this country, approximately 15,000 are blind because of corneal opacities. The latter stand a good chance of having their sight restored or improved by a corneal transplant from an eye removed within one hour of death and used within seventy-two hours. Although the group represents only a small percentage of those who are blind, the possibilities for beneficial results are impressive.

If the eye is not used within seventy-two hours, is it wasted? By no means. The eyes of mammals other than man are not entirely satisfactory for histologic, anatomic and physiologic studies, and yet such investigations must be carried out if the human race is to benefit. An intact human eye that could not be used for a corneal transplant might be ideal for certain studies, since it is presumably free from major defects and clearly has the properties common to other human eyes, except, of course, lack of circulation. Another important use for these eyes would be the training of ophthalmic residents in surgical procedures. This would be far superior to the present custom of employing animal eyes.

If these two misconceptions could be cleared up in the lay mind, the Eye Bank at the Massachusetts Eye and Ear Infirmary would probably prosper even better than it now does.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

BURGER — Franklin D. Burger, M.D., of Wellesley Hills, died November 25. He was in his forty-seventh year.

Dr. Burger received his degree from University of Michigan Medical School in 1936.
His widow survives.

SYLVESTER — Albion W. Sylvester, M.D., of Pittsfield, died June 20. He was in his eighty-fourth year.
Dr. Sylvester received his degree from Bowdoin Medical College in 1892.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

ANTIPNEUMOCOCCUS SERUM FOR SEVERE PNEUMOCOCCAL INFECTIONS

Occasional requests are still received by the Department of Public Health for antipneumococcus serum. Most of these relate to cases of pneumococcal meningitis, a disease with such a high fatality rate, even under optimal conditions, that serum is generally regarded as an imperative adjunct to chemotherapy. The department will therefore continue to furnish antipneumococcus serum until such time as serum has been found to be superfluous in the treatment of severe pneumococcal infections.

Because of the small number of requests, all serum depots have been discontinued except the one at the Bacteriological Laboratory, State House, where 100,000-unit vials of Types 1 to 33, inclusive, are kept available. The issue of serum will continue to be based on the following provisions:

The pneumococcus must be typed in a laboratory approved for this diagnostic procedure by the Department of Public Health or in a federal laboratory.

The patient must be suffering from pneumococcal pneumonia, septicemia, endocarditis, meningitis or peritonitis.

Serums for Types 1, 2, 4, 5, 7, 8, 9, 14 and 18 will be furnished for treatment of the above conditions on type identification of the pneumococcus, regardless of whether it has been isolated from the sputum, throat or elsewhere.

Serums for other types will be furnished only when the organism is found in the blood, cerebrospinal fluid or peritoneal fluid.

Unused serum must be properly refrigerated and returned as promptly as possible to the Division of Biologic Laboratories, 375 South Street, Jamaica Plain 30.

When the patient is discharged, a case history on the form provided must be filled out and sent to the Division of Biologic Laboratories.

CORRESPONDENCE

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held November 22, it was voted to restore the certificate of registration of Dr. Theodore Rosen, formerly of 45 Joy Street, Boston.

H. QUIMBY GALLUPE, M.D., Secretary

State House
Boston

NOTICES

ANNOUNCEMENTS

Dr. Hugh C. Donahue calls attention to the omission of his office address and telephone number from the current telephone directory. His office continues to be at 520 Commonwealth Avenue, Boston, and the telephone number is COM monwealth 2010.

Dr. William T. Haley, Jr., who has returned from military service, announces the opening of his office for the general practice of medicine at 79 Pleasant Street, Marblehead.

(Notices continued on page xvii)

weak and scanty. The blood pressure gradually fell to 80/40. Despite sulfonamide medication the temperature continued to fluctuate between 99.5 and 101°F. The serum nonprotein nitrogen rose to 264 mg per 100 cc. The patient's breathing became stertorous and labored, and he lapsed into coma and died on the 8th hospital day.

Autopsy. On gross examination the combined weight of the kidneys was 650 gm. The cortices were studded with abscesses, 0.1 to 0.5 cm in diameter, and in several areas pus had accumulated beneath the capsule in amounts up to 10 cc. On section, similar abscesses were seen scattered throughout the parenchyma, but in addition two or three papillae of each kidney were replaced near their tips by soft, yellow-green areas of necrosis. The prostate was bilaterally enlarged to approximately twice its normal size, and in the mid-

PATHOLOGIC ANATOMY

The gross and microscopic pictures of this lesion are remarkably constant, varying only in degree according to the stage it has reached when seen. The findings are not influenced essentially by different etiologic organisms and show no difference in the diabetic and nondiabetic groups.

Grossly, the earliest stage consists of scattered small abscesses located in the renal pyramid, more or less in a line parallel to the cortex at a level about

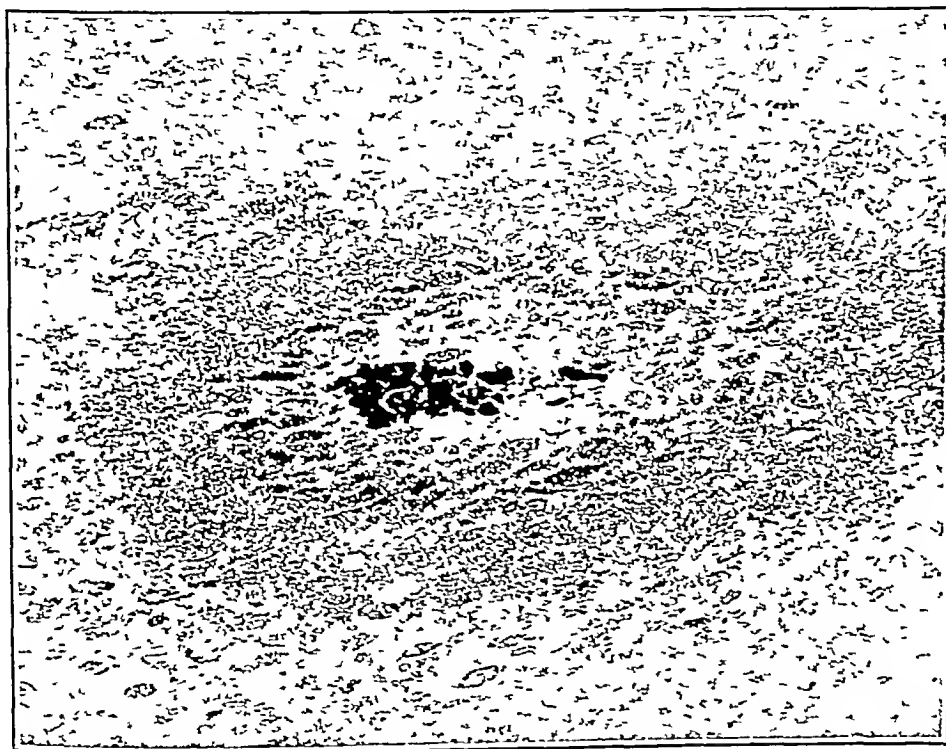


FIGURE 1 Photomicrograph of Early Lesion of Pyramid

there was a 1-cm ball-valve-like projection from the median bar obstructing the neck of the urethra. Serial sections of the prostate revealed several 0.5-cm areas of abscess formation. Bacteriologic examination was somewhat unsatisfactory, since cultures of the spleen, prostate and kidney obtained *Proteus vulgaris* that overspread the culture plates and masked all other growth.

The anatomical diagnoses were acute pyelonephritis, with encroaching papillitis, benign prostatic hypertrophy, acute and chronic prostatitis and hypertensive and arteriosclerotic heart disease, with decompensation.

This patient represented one of the nondiabetic patients who, in the wake of urinary-tract obstruction, developed an acute renal infection. The strategically located necrosis of the papillae superimposed on the fairly widespread cortical damage sufficed to produce acute renal failure, uremia and death in the relatively short time of eight days.

two thirds the way from the tip of the papilla to the junction of the pyramid and the cortex (Fig. 1). As the lesion progresses, these abscesses become confluent, resulting in a complete necrosis of the terminal two thirds of the pyramid. The appearance of the necrotic tissue is somewhat similar to that of an infarct of the cortex, except that it is apt to be yellow brown or yellow green, with the periphery sharply demarcated by a narrow zone of paler yellow-to-green tissue, which in turn may be surrounded by a border of reddish congestion. Varying amounts of the more usual type of acute pyelonephritis are found in the cortex of these kidneys. The process is frequently but not always bilateral, and in most cases all pyramids of the affected kidney are involved (Fig. 2).

and a fluctuant abscess, measuring 60 x 40 x 20 cm, in the left popliteal space. Hemolytic *Staph aureus* was cultured from both the blood and the kidneys.

The anatomical diagnoses were diabetes mellitus, as evidenced by the clinical findings and glycogen nephrosis, acute pyelonephritis, with necrotizing papillitis, a healing abscess over the left ankle and an abscess in the left popliteal space.

This case represented the insidious onset, in a diabetic patient, of renal infection secondary to focal infection elsewhere in the body. Death was attributed to a combination of severe infections of the leg and kidneys, neither of which alone could be considered as a fatal disease.

CASE 2 B C (BCH 1,161,259), a 68-year-old woman, entered the hospital with a left hemiplegia. Eight days previously she had experienced the sudden onset of transient left facial weakness and difficulty in talking. Several similar episodes occurred in the next few days. The patient sought hospitalization for relief of the complete unilateral paralysis. She was known to have had diabetes for 15 years, which had been controlled by diet alone.

Physical examination revealed an obese, flushed, restless woman with an obvious left hemiplegia. The lungs contained scattered moist rales posteriorly with bronchial breathing. Except for slight enlargement to the left, the heart was not remarkable. No signs of any infection, renal or otherwise, were demonstrable.

Examination of the urine demonstrated a trace of albumin and a green Benedict reaction. The fasting blood sugar was 196 to 270 mg per 100 cc. The serum nonprotein nitrogen was 42 mg per 100 cc on admission.

Soon after entry it became apparent that the left hemiplegia was of secondary importance to a rapidly developing urinary infection. *Klebsiella pneumoniae* (Type B) was cultured from the urine. The serum nonprotein nitrogen rose progressively to over 100 mg per 100 cc. Blood cultures, which at first were sterile, soon became positive for *K pneumoniae*. The temperature rose to 103°F. Various sulfonamides were administered without effect. The urinary output began to fail, and the patient lapsed into coma and died.

Autopsy On gross examination the combined weight of the kidneys was 330 gm. The cortical surfaces were studded with minute abscesses, 0.2 to 0.3 cm in diameter. On section of both kidneys most of the papillae were completely replaced by green, semifluid areas of necrosis. These areas were roughly wedge shaped, with their bases at the corticomedullary junction. The calyces and pelvises were filled with mucoid, green exudate. The brain showed moderate arteriosclerosis of the cerebral vessels, with thrombosis of the right middle cerebral artery and infarction of the right frontal, parietal and temporal lobes. Other pertinent findings were bilateral lower-lobe bronchopneumonia and an early adenocarcinoma of the colon. *K pneumoniae* was cultured from the heart's blood, kidneys and lungs.

The anatomical diagnoses were acute pyelonephritis, with necrotizing papillitis, diabetes mellitus (clinical), cerebral thrombosis, with encephalomalacia, of the right frontal, parietal and temporal lobes, bilateral bronchopneumonia of the lower lobes and carcinoma of the colon.

This elderly woman was admitted to the hospital after an obvious right cerebral vascular accident with evidence of a developing urinary-tract infection with *K pneumoniae* (Type B) and no other demonstrable focus of infection. In the course of seven weeks, the serum nonprotein nitrogen rose to over 100 mg per 100 cc. The patient became anuric and died in uremia. The urinary-tract infection apparently developed in the absence of any demonstrable focus of infection.

CASE 3 J G (BCH 1,164,454), a 55-year-old man, was admitted to the hospital in a state of stupor. The history obtained from his wife indicated that he had developed a "cold" 2 weeks before entry and had subsequently suffered

from a cough with occasional bouts of feverishness followed by shaking chills. No past or present history referable to diabetes mellitus was obtained.

Physical examination disclosed a moderately cyanotic man who was obviously extremely ill, was only garbled, inarticulate words. A few fine, moist wheezes were heard over the lung posteriorly. The heart was slightly enlarged, and there was a Grade II systolic murmur over the apex. There was no costovertebral-angle tenderness.

Examination of the urine showed a green Benedict reaction, no albumin was demonstrated despite the finding of 50 to 100 white cells per high-power field. The fasting blood sugar was 286 mg, and the serum nonprotein nitrogen 67 mg per 100 cc.

On the 2nd hospital day petechiae were noted over the extremities, the temperature rose to 106°F, and the respirations became labored. A beta-hemolytic streptococcus was isolated from the blood. The serum nonprotein nitrogen was 92 mg, and the fasting blood sugar 475 mg per 100 cc. Despite penicillin and sulfonamide the temperature remained elevated. The patient became anuric, the blood pressure dropped to 80/0, and he expired 70 hours after admission.

Autopsy On gross examination the combined weight of the kidneys was 630 gm. The capsular surfaces were relatively smooth and uniformly red brown, and there were no abscesses. On section there were numerous areas of yellow-white, puriform necrosis within the pyramids, involving almost all the papillae and in some extending from the cortex to the tip of the papilla. The medullary zones of the adrenal glands were red and hemorrhagic. The lungs and heart were essentially normal. The liver weighed 2750 gm and showed a diffuse yellow-brown nodularity, with many individual nodules up to 1 cm in diameter, section of the liver showed the parenchyma to be traversed by fine fibrous trabeculae. The spleen was enlarged, weighing 560 gm, but was otherwise not remarkable. A streptococcus with alpha to beta hemolysis was cultured from the heart's blood and kidneys.

The anatomical diagnoses were diabetes mellitus, as evidenced by the clinical findings and glycogen nephrosis, acute pyelonephritis, with necrotizing papillitis, and alcoholic cirrhosis of the liver.

This case, which occurred in a previously unsuspected diabetic patient, represented the disease in one of its most fulminating forms, the marked febrile illness and septicemia having had their origin in the renal infection. Petechiae of the skin, as well as adrenal medullary hemorrhages, simulating the Waterhouse-Friderichsen syndrome, were present. No other focus of infection was demonstrated at autopsy, and the renal lesion was the chief cause of both the clinical picture and death.

CASE 4 J R (BCH 1,058,331), a 68-year-old man, was admitted to the hospital for the second time within a period of 5 days because of acute urinary retention. On the previous admission he had also entered for acute retention, but had refused operation for removal of an obstructing prostate and had left the hospital against advice. He remained at home during this interval with no urinary difficulty until the day of re-entry. He stated that the first urinary symptoms had begun 4 months before admission. There was no history indicative of diabetes mellitus.

Physical examination revealed an elderly man lying quietly in no distress. The lungs were clear and resonant throughout. Examination of the heart revealed slight enlargement in the left, with an irregularity suggesting auricular fibrillation. The urinary bladder was palpated at the level of the umbilicus, and on rectal examination the prostate was large, symmetrical and firm.

Examination of the urine demonstrated a trace of albumin, no sugar and many white cells per high-power field. The serum nonprotein nitrogen was 59 mg, and the fasting blood sugar 108 mg per 100 cc.

After catheterization the patient appeared to be comfortable and well until the 2nd hospital day, when the temperature suddenly rose to 101°F and he became somewhat stuporous and disoriented. The urine, which had been fairly clear and adequate in amount on entry, became foul smelling

DISCUSSION

The most striking feature of necrotizing pyelonephritis is its frequent association with diabetes mellitus, in this series of 26 autopsied cases, 19 patients were diabetic. This distribution assumes even greater significance when it is realized that during this period of study approximately 10,000 autopsies were performed in these laboratories, of which approximately only 400 were performed on diabetic patients. It is essential, however, to emphasize the fact that although the disease is more characteristic of diabetic patients, it is also found in those without diabetes. Since the clinical features of the two groups differ somewhat, they are discussed separately.

In diabetes mellitus, acute pyelonephritis is a frequent complication, occurring in 60 patients in a series of approximately 307 diabetic patients who were autopsied at one of these laboratories.⁶ Necrotizing papillitis was present in 16 of these 60 cases.

the lesion developed post partum, so that no age group is immune to this disease. In the diabetic group women outnumber men 12 to 7.

The clinical courses appeared to assume one of two relatively constant patterns, which for the purposes of discussion can be categorized as "acute fulminating" and "subacute protracted." Patients in the former group frequently entered the hospital seriously ill with a sudden onset of symptoms suggestive of a severe generalized systemic infection. A rapidly fatal course developed, characterized by prostration, spiking, high temperature, rapid pulse and occasionally leukocytosis in the complete absence of clinically demonstrable foci of infection. Invariably marked pyuria and oliguria were present with associated azotemia. Most of these patients died within a period of days, one within four days of the onset of the illness. Death resulted either from uremia or from overwhelming infection. One patient suffered from systemic infection of such

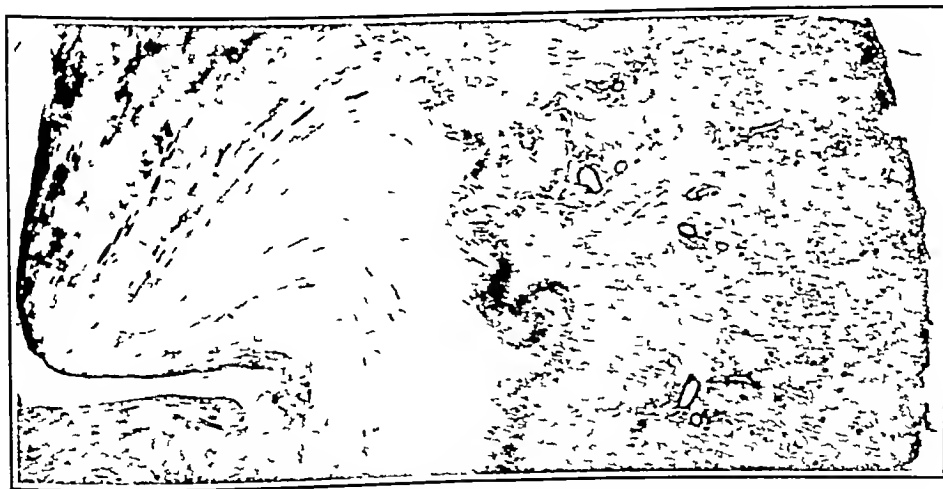


FIGURE 3 Photomicrograph of Cortex and Pyramid, Showing the Distribution of a Well Developed Lesion

of acute pyelonephritis, producing the rough proportion in diabetic patients of 1 case of necrotizing pyelonephritis to every 4 of acute suppuration of the kidney. In terms of the frequency with which necrosis of the renal papillae is found in post-mortem examination of diabetic patients, the incidence is approximately 4.5 per cent. Some of the significant features of these cases, both clinical and pathological, have been summarized in Tables 1 and 2.

It is apparent that this lesion was found in diabetic patients of nearly every age group, the youngest patient being thirty-nine and the oldest eighty-one years old. The decade in which this pathologic entity was encountered most frequently in our series, however, was the seventh. Sheehan⁷ reported a case in an eighteen-year-old girl in which

severity that clinically the case was first thought to be acute bacterial endocarditis with petechial skin lesions, adrenal medullary hemorrhages were demonstrated at post-mortem examination.

In the "subacute protracted" cases there was usually a period of weeks and months of pyuria and obvious acute pyelonephritis, during which the disease appeared to undergo remissions and exacerbations. Invariably the patient's condition suddenly became critical, the pyuria growing more marked, and the disease followed a course resembling the acute type, progressing rapidly to a fatal termination. After pathological study of the kidneys in these cases, it seems possible to explain this course of events as one in which necrotizing papillitis was superimposed on a pre-existing nonspecific acute

In more advanced lesions portions of the involved papillae break off into the lumen of the pelvis, and complete sequestration may occur with sloughing of the whole papilla into the pelvis. If such a stage is reached during life, a fairly characteristic deformity of the pelvis can be seen on pyelography.

As would be expected from this gross description, the histology also varies with the age of the lesion. The earliest stage, as seen in the experimental pyelonephritis of the rabbit, consists in clumps of organisms in the interstitial tissue that provoke a

the pyramid consists of arterial capillaries lead down and venous capillaries leading up the pyramid with only poor anastomotic connections. It is probable that as a result of inflammation the afferent blood supply is greatly hindered, with consequent infarction.

In the well developed lesion the papillae are completely involved (Fig 3). At the base of the pyramid there is a zone composed of masses of organisms lying in capillaries, tubules, lumens and interstitial tissue and surrounded by large numbers of polymorphonuclear leukocytes. In this zone, scattered



FIGURE 2 Gross Appearance of Sectioned Kidney of a Diabetic Patient, Showing Well Advanced, Typical Pyramidal Lesions

polymorphonuclear leukocytic reaction, with necrosis and eventual rupture into the nearby tubules. In human beings probably the majority of abscesses start in a similar manner in the interstitial tissue, but the possibility that they may begin in the lumens of the tubules cannot be ruled out.

As the abscesses enlarge, or if two or more become confluent, a small area of infarct necrosis is likely to develop in the region below—that is, distal to the area involved—and to spread almost to the tip of the papilla. This is probably best explained by the circulation of the pyramid. In a normal kidney no blood vessels larger than capillaries are found in the distal two thirds of the pyramid, and apparently the entire blood supply of

capillaries contain fibrin thrombi and above this area the capillaries are found to be dilated and engorged. A similar zone of inflammatory infiltration—but without organisms or capillary thrombi—often extends around the complete periphery of the involved pyramid. The central portions of the papilla show infarct necrosis with pyknosis or loss of cell nuclei but maintenance of normal architecture, and there is little or no inflammatory infiltration. The further evolution of the lesion consists merely of a loss or disappearance of the necrotic tissue, only the zone of infiltrated tissue remaining near the base of the pyramid.

To date the healed stage, if healing does occur, has not been recognized.

Discussion

The most striking feature of necrotizing pyelonephritis is its frequent association with diabetes mellitus, in this series of 26 autopsied cases, 19 patients were diabetic. This distribution assumes even greater significance when it is realized that during this period of study approximately 10,000 autopsies were performed in these laboratories, of which approximately only 400 were performed on diabetic patients. It is essential, however, to emphasize the fact that although the disease is more characteristic of diabetic patients, it is also found in those without diabetes. Since the clinical features of the two groups differ somewhat, they are discussed separately.

In diabetes mellitus, acute pyelonephritis is a frequent complication, occurring in 60 patients in a series of approximately 307 diabetic patients who were autopsied at one of these laboratories.⁶ Necrotizing papillitis was present in 16 of these 60 cases

the lesion developed post partum, so that no age group is immune to this disease. In the diabetic group women outnumber men 12 to 7.

The clinical courses appeared to assume one of two relatively constant patterns, which for the purposes of discussion can be categorized as "acute fulminating" and "subacute protracted." Patients in the former group frequently entered the hospital seriously ill with a sudden onset of symptoms suggestive of a severe generalized systemic infection. A rapidly fatal course developed, characterized by prostration, spiking, high temperature, rapid pulse and occasionally leukocytosis in the complete absence of clinically demonstrable foci of infection. Invariably marked pyuria and oliguria were present with associated azotemia. Most of these patients died within a period of days, one within four days of the onset of the illness. Death resulted either from uremia or from overwhelming infection. One patient suffered from systemic infection of such

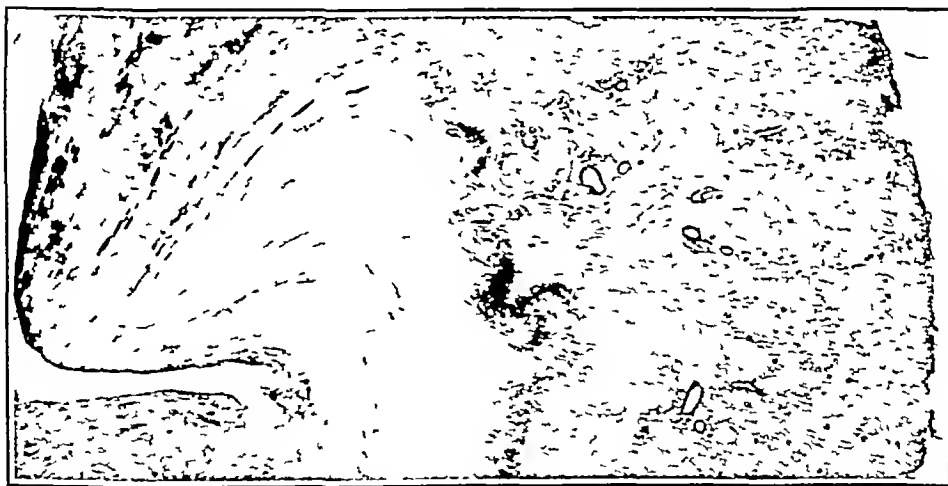


FIGURE 3 Photomicrograph of Cortex and Pyramid, Showing the Distribution of a Well Developed Lesion

of acute pyelonephritis, producing the rough proportion in diabetic patients of 1 case of necrotizing pyelonephritis to every 4 of acute suppuration of the kidney. In terms of the frequency with which necrosis of the renal papillae is found in post-mortem examination of diabetic patients, the incidence is approximately 4.5 per cent. Some of the significant features of these cases, both clinical and pathological, have been summarized in Tables 1 and 2.

It is apparent that this lesion was found in diabetic patients of nearly every age group, the youngest patient being thirty-nine and the oldest eighty-one years old. The decade in which this pathologic entity was encountered most frequently in our series, however, was the seventh. Sheehan⁷ reported a case in an eighteen-year-old girl in which

severity that clinically the case was first thought to be acute bacterial endocarditis with petechial skin lesions, adrenal medullary hemorrhages were demonstrated at post-mortem examination.

In the "subacute protracted" cases there was usually a period of weeks and months of pyuria and obvious acute pyelonephritis, during which the disease appeared to undergo remissions and exacerbations. Invariably the patient's condition suddenly became critical, the pyuria growing more marked, and the disease followed a course resembling the acute type, progressing rapidly to a fatal termination. After pathological study of the kidneys in these cases, it seems possible to explain this course of events as one in which necrotizing papillitis was superimposed on a pre-existing nonspecific acute

TABLE 1 Data in 19 Diabetic Patients with Necrotizing Papillitis

PATIENT	AGE	SEX	KNOWN DURATION OF DIABETES	HIGHEST FASTING BLOOD SUGAR	EXTRARENAL INFECTION	DURATION OF PYEMIA	CLINICAL EVIDENCE OF UREMIA	ANTEMORTEM BLOOD CULTURE	ANTEMORTEM URINE CULTURE	POSTMORTEM KIDNEY CULTURE	COMBINED WEIGHT OF KIDNEYS	URINARY-TRACT OBSTRUCTION	CAUSE OF DEATH
S F	61	F	3 yr	381 mg/100 cc	Cellulitis of left leg	2 mo	—	<i>Staph aureus</i>	—	<i>Staph aureus</i>	300 gm	None	Rising nonprotein nitrogen, coma and probable uremia
J G	55	M	—	475	None	2 days	Anuria	Alpha-beta streptococcus	—	Alpha beta streptococcus	630	None	Adrenal hemorrhage, high fever and fulminating infectum
J F	81	M	5	242	Meningitis	—	—	—	—	—	330	None	Meningitis
M M	63	F	6	—	None	4 days	Nonprotein nitrogen of 80 mg per 100 cc (rising)	—	—	<i>Esch coli</i>	320	None	Progressive azotemia and uremia
A S	69	F	13	303	None	2 days	None	—	—	<i>Staph aureus</i> and <i>Esch coli</i>	250	None	Myocardial infarctum
M H	45	F	8	345	None	2 wk	Nonprotein nitrogen of 130 mg per 100 cc (rising)	—	<i>Pr vulgaris</i>	<i>Pr vulgaris</i> and alpha streptococcus	600	None	Progressive azotemia and uremia
J C	68	M	8	150	None	—	None	<i>Esch coli</i>	—	<i>Esch coli</i> , <i>Staph aureus</i> and alpha streptococcus	600	None	High fever and infection
N M	52	M	—	300	Osteomyelitis of toe	—	None	<i>Staph aureus</i>	—	<i>Staph aureus</i>	520	None	High fever and septicemia
F J	47	F	15	500	None	Years	Marked anuria	—	—	—	370 (left only)	None	Progressive azotemia, anuria and uremia
D R	59	I	—	308	Carbuncle of neck	8 days	None	<i>Staph aureus</i>	—	<i>Staph aureus</i>	320	None	Suppurative pancreatitis
A C	55	M	15	251	Empyema	3 mo	None	—	—	<i>Staph aureus</i>	350	None	Empyema
B C	68	F	6	500	None	2 mo	None	<i>K pneumoniae</i>	<i>A pneumoniae</i>	<i>A pneumoniae</i>	330	None	Septicemia
C C	59	F	7	200	None	Years	Nonprotein nitrogen of 235 mg per 100 cc anuria	—	—	—	140 (right only)	None	Metastatic carcinoma with uremia
J K	72	M	2	500	—	—	Coma	—	—	—	380	Moderately enlarged prostate	Progressive azotemia and uremia
J W	60	F	—	—	None	Weeks	—	<i>Pr aeruginosa</i>	<i>Pr aeruginosa</i>	<i>Pr aeruginosa</i>	650	None	Progressive azotemia and uremia
A F	50+	F	—	—	Pneumonia	Days	None	<i>Staph aureus</i>	—	<i>Staph aureus</i>	450	None	Infectum with pneumonia and severe renal apnea
F D	39	M	10	202	Carbuncles	6 mo	None	<i>Staph aureus</i>	<i>Staph aureus</i>	<i>Staph aureus</i>	470	None	Acute yellow atrophy
E B	46	F	—	350	None	8 mn	Nonprotein nitrogen of 70 mg per 100 cc	Nonhemolytic ataphylococcus	—	<i>Esch coli</i> and streptococcus	600	None	Progressive azotemia and uremia
E F	46	F	—	—	—	5 days	Nonprotein nitrogen of 95 mg per 100 cc	<i>Esch coli</i>	<i>Esch coli</i>	<i>Esch coli</i>	—	None	Progressive azotemia and uremia

pyelonephritis as an apparently terminal complication coinciding with the sudden increase in the gravity of the clinical picture. This lesion did not lead to death in every case, since 5 patients died of unrelated causes (Table 1). Moreover, 2 diabetic patients were studied in each of whom a kidney showing necrotizing pyelonephritis was removed. Both progressed well postoperatively and were apparently free of renal disease a year later. Whether these cases represent examples of extremely rare unilateral necrotizing pyelonephritis in diabetic

This was borne out by the fact that the diabetes present in several of the patients in this series was so mild that it was controlled by diet alone.

Necrotizing papillitis was also present in 7 patients who did not have diabetes. All these patients were men between the ages of sixty-one and seventy-one (Table 2).

The small number of nondiabetic patients with necrosis of the renal papillae, despite the large number of autopsies performed on nondiabetic patients (in the neighborhood of 10,000), is in keeping with

TABLE 2 Data in 7 Nondiabetic Patients with Necrotizing Papillitis

PATIENT	AGE	SEX	EXTRA-RENAL INFECTION	DURATION OF PYURIA	CLINICAL EVIDENCE OF UAEMIA	ANTE-MORTEM BLOOD CULTURE	ANTE-MORTEM URINE CULTURE	POST-MORTEM KIDNEY CULTURE	COMBINED WEIGHT OF KIDNEYS	URINARY-TRACT OBSTRUCTION	CAUSE OF DEATH
W. B.	62	M	None	1 mo.	Nonprotein nitrogen of 80 mg per 100 cc (rising)	—	—	<i>Esch. coli</i> and alpha streptococcus	300 gm	Marked amorphous crystals in ureters	Progressive azotemia and uremia
J. C.	61	M	None	6 days	Nonprotein nitrogen of 144 mg per 100 cc.	<i>Esch. coli</i>	<i>Esch. coli</i>	<i>Esch. coli</i>	340	—	Progressive azotemia and uremia
A. F.	61	M	Prostatic abscesses	10 days	Nonprotein nitrogen of 220 mg per 100 cc and anuria	—	<i>K. pneumoniae</i>	<i>K. pneumoniae</i>	600	Moderate enlargement of prostate	Uremia rapid course
G. S.	67	M	None	9 days	Nonprotein nitrogen of 222 mg per 100 cc. (rising)	—	—	Overgrown by <i>Pr. vulgaris</i>	650	Enlarged prostate	Progressive azotemia and uremia
J. R.	68	M	None	8 days	Nonprotein nitrogen of 190 mg per 100 cc. and anuria	<i>Pr. vulgaris</i> (pure culture)	—	Heart's blood, kidney and urine, <i>Pr. vulgaris</i> (pure culture)	580	Moderate enlargement of prostate	Progressive azotemia and uremia
E. S.	71	M	None	10 days	Nonprotein nitrogen of 250 mg per 100 cc. and anuria	—	—	Heart's blood and kidney, <i>Pr. vulgaris</i> (pure culture)	350	Enlarged prostate	Progressive azotemia and uremia
M. G.	71	M	None	3 days	Nonprotein nitrogen of 200 mg per 100 cc. and anuria	—	—	—	450	Enlarged prostate	Progressive azotemia and uremia

patients is uncertain, but it is probable. The likelihood that the remaining kidney was involved to an equally severe extent and then healed to give adequate renal function alone appears to be remote, for reasons discussed below.

Not one of the cases studied presented any signs or symptoms referable to urinary-tract obstruction, partial or complete—a finding corroborated by pathological examination. This absence of urinary-tract stasis stands out in sharp contrast to the findings in the nondiabetic patients, most of whom had some symptoms referable to urinary-tract obstruction, usually those of prostatic enlargement.

The degree of severity of the diabetes did not appear to be a factor in the pathogenesis of the lesion.

The rarity of this lesion in patients without diabetes. During the period of study in which 7 typical examples of papillary necrosis were found, 93 cases of fairly marked, significant amounts of nonspecific acute pyelonephritis were encountered. The advanced age of these patients, as well as the striking dominance of the male sex, is closely related to the fact that the urinary-tract obstruction that frequently underlies these cases is almost invariably due to an obstructing prostate. It is interesting to note that necrosis of the renal papillae has been reproduced experimentally by Mallory et al.⁷ in nondiabetic rabbits by the ligation of one ureter and intravenous injection of organisms. In the non-obstructed kidney no significant lesions developed,

in the obstructed kidney an acute pyelonephritis with necrosis of the renal papillae, as well as cortical abscesses, was found — the exact analogue of the lesion found in the nondiabetic group discussed above, in which the necrotizing papillitis proved to be the cause of death, leading to a rapidly rising nonprotein nitrogen, terminal anuria with uremia.

Considering the series once again as a whole, including both diabetic and nondiabetic patients, it is apparent that in 20 out of the 26 cases at autopsy (Tables 1 and 2), death was directly attributable to the development of the papillitis, representing a mortality rate of 74 per cent, the proportion of deaths being equally divided between the diabetic and the nondiabetic patients.

It became apparent on the review of the clinical material that correct diagnosis of this type of renal lesion was rarely made before death. In only 1 case was the pyramidal, necrotizing character of the renal infection suspected prior to death, although in many cases, chiefly in the more protracted ones, the obvious urinary-tract infection was well recognized and under active therapy. The acute fulminating cases created the most confusing diagnostic problems, and such divergent diagnoses as bacterial endocarditis, perinephric abscess and pneumonia were made.

Clinically, this lesion should be suspected in any severe, acute infection of the urinary tract in both diabetic and nondiabetic patients with urinary obstruction, especially if there is an associated oliguria and rapidly rising nonprotein nitrogen. In suspected cases a retrograde pyelogram may demonstrate an irregular filling defect of the renal calyces that is due to necrosis and sloughing of the tips of the papillae.⁸ The changes in the pyelograms are not unlike those seen in renal tuberculosis.

Despite the high mortality in these cases, the correct ante-mortem diagnosis is of more than academic interest, since the lesion has two characteristics that dictate specific therapy. It is a suddenly developing and rapidly progressing, necrotizing bacterial lesion that must be treated not only actively but without delay. In addition, the strategic necrosis of the tips of the papillae impairing the urinary drainage of the associated nephrons may create a significant hazard to the use of sulfonamide compounds with their known tendency to precipitate out in the renal tubule under conditions of urinary stasis.⁹

It is to be stressed that necrotizing papillitis is simply a form of acute pyelonephritis in which the chief damage occurs within the pyramids, frequently destroying, in the severer cases, practically every pyramid. These areas of medullary necrosis are usually, but not invariably, found together with abscess formation within the cortex.

In the sections of the kidney lesions studied, as well as in all the cases that have come under study at these laboratories, no recognizable chronic or

healed papillary necrosis has been encountered. This fact leads to the conclusion that the cases either are invariably fatal or would have been if death had not been intercurrent. The failure to encounter a chronic or healing lesion makes it unlikely that this disease can heal. For these reasons, the 2 nephrectomized patients in whom papillary necrosis was found in the removed kidneys were thought to represent unilateral involvement. All the papillary lesions examined histologically were acute and sometimes were found in the presence of chronic nonspecific pyelonephritis, indicating that the papillary necrosis was preceded by the cortical changes and probably represented a superimposed terminal complication.

As can be seen from the tables, a great variety of bacterial agents were isolated in these cases, *Staph aureus*, *Escherichia coli*, *K pneumoniae* and *Streptococcus viridans* being the most frequent. It is, however, almost possible to predict the type of organism that will be found by an analysis of the clinical course of the case. Patients who entered with obvious foci of infection outside the kidney almost invariably developed staphylococcal and streptococcal renal infections, and in those in whom no definite preceding infection could be demonstrated the organisms cultured from the kidney were usually *Esch coli* and *K pneumoniae*. In many cases, however, mixed bacterial infections were found, and it can only be assumed that some of the complexity of the culture reports resulted from secondary or even post-mortem bacterial invaders.

The pathogenesis of the lesion has for years interested pathologists. The great variety of theories that have been offered in explanation of this infrequent type of kidney infection bears eloquent testimony to the fact that to date no adequate pathogenesis has been described.³

Although we have no new hypothesis to advance, certain features of the histologic picture seem to be more consistent with one of these hypotheses than with the others. Certainly, the infarct-like necrosis of the lesion suggests that ischemia of the pyramids is important in the development of the lesion. Moreover, papillary ischemia as the cause of this necrosis best explains the occurrence of the lesion in the apparently widely divergent group of diabetic patients with no urinary obstruction and in nondiabetic patients with urinary obstruction.

In both groups, capillary thromboses, marginal inflammation and masses of bacteria are demonstrable. But in the diabetic cases the greater amount of reaction, with the massive bacterial aggregates and marked cellular exudate, apparently compresses and collapses the thin-walled, capillary-like channels that traverse the pyramid between the tubules. In the nondiabetic group, whereas the inflammatory reaction is less marked and internal pressure is therefore less, the added factor of urinary obstruction and hydronephrotic pressure externally about the

pyramid and within the tubules seems to make up for this decrease in internal pressure within the papilla

It can thus be seen that the apparently widely differing clinical circumstances, such as diabetes and urinary-tract obstruction, actually produce essentially the same disturbance in the normal physiology of the kidney — reduction in papillary blood supply to the point of infarction

SUMMARY

Twenty-six autopsied cases of necrotizing papillitis of the renal pyramids are presented from both the clinical and pathological viewpoints, 19 of which occurred in diabetic and the remainder in non-diabetic patients. It is to be emphasized that this lesion is a frequent type of acute pyelonephritis in diabetic patients. It is seen far more rarely in non-diabetic patients and when present is associated with urinary-tract obstruction.

Clinically the cases divide themselves into a "fulminating" and a "subacute" group. In the former the presenting syndrome was one of the sudden onset of severe systemic infection, often without localizing signs. The "subacute" cases usually had obvious acute pyelonephritis for weeks to months until, without apparent prodromal symptoms, the urinary-tract infection became much severer and the course assumed the character of the "fulminating" cases.

Viewing both groups as a whole, most of the patients died of rapidly progressing uremia — 8 in the diabetic group and all 7 of the nondiabetic patients. Some of the former, however, showed little renal insufficiency and died of overwhelming infections.

In 74 per cent of the cases studied the death of the patient could be attributed primarily to this specific renal lesion.

Pathologically the lesion is readily recognized by the pale yellow-white, infarct-like necrosis of the papillae, bordered above by a green-to-red zone of inflammatory reaction.

The pathogenesis of this lesion is uncertain and appears to be unrelated to any specific bacteria. It probably represents a severe type of inflammatory renal disease to which the diabetic patient and the patient with urinary-tract obstruction are peculiarly susceptible.

Ante-mortem clinical diagnosis of this lesion, which is rarely made, is frequently possible only if the lesion is considered and if, in the presence of obvious urinary-tract infection, a rapidly rising non-protein nitrogen and anuria are encountered, especially in diabetic patients. In the later stages characteristic pyelographic changes are often demonstrated.

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ANOXIA NEONATORUM*

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OLIVER Wendell Holmes, lecturing in anatomy to the students at Harvard Medical School, held aloft the skeleton of a female pelvis and delineating the pubic arch, said, "This, gentlemen, is the triumphant arch, beneath which all heroes must pass as the first hazard to be overcome along the path to their ultimate coronation." Dr Holmes apparently gave little consideration to birth by cesarean section, but today it is known that that particular method of entrance into this world is not without its inherent perils to incipient heroes. I doubt whether Holmes was cognizant of the problems of anoxia, but then, as now, babies were born destroyed, as in death, and born mutilated, by partial irreparable damage, owing to oxygen lack during the accomplishment of their birth, he recognized this fact in his romantic description of that particular portion of the female pelvis.

In the present state of incomplete knowledge of the inaccessible and parasitical fetus, the distinction between the physiologic and the pathologic is indeed narrow. As a basic fact, it is known that adequate oxygenation of the tissues must be maintained if life is to remain in the body and that, whatever the inciting cause of a lethal syndrome, it is ultimately lack of oxygen availability or utilization that kills or maims. This is the one common denominator in all fetal deaths and permanent injuries. Anoxia, it is extremely important to realize, results not only from failure of respiration at birth, although this, of course, is the most frequent cause, but also from a series of pathologic events that may start at the time of nidation of the fertilized egg, with the formation of an inadequate placenta, or that may occur at any time during the prenatal, transnatal or postnatal period.

Clifford,¹ in a careful and well documented account of anoxemia, substantiated by complete obstetric, pediatric and autopsy records, has demonstrated the general pathologic effects involving the whole organism as a result of oxygen lack, even though symptoms referable to one part of the body, such as pulmonary atelectasis and intracranial injury, dominate the picture. The essential pathologic changes due to anoxia are summarized as congestion, edema, hemorrhage and, finally, tissue degeneration. The actual symptoms encountered, as well as their severity, depend on the degree and duration of anoxia and on the susceptibility of individual tissues affected. At one end of the scale,

these changes lead to death and from this point on there is a gradation of effect, through the symptomatology due to outright destruction of nerve tissue up to impairment of intelligence. This point was well demonstrated by Darke,² who in a study of the intelligence quotients of children who had suffered from acute oxygen lack at birth in comparison with those of their parents and siblings, showed that as a rule such children were retarded in later life. Preston,³ in a similar investigation, demonstrated arrest and interference with physical, nervous, mental, emotional and personality development from the same cause.

The responsibility for stillbirth and natal and neonatal mortality and morbidity is a joint one of the obstetrician and the pediatrician, nursing care providing the most important aspect of either effort. The pediatricians are to be complimented for their excellent progress with their end of the bargain. The main difficulty confronting the obstetrician is the completely normal course of most of his cases, which in turn causes an individual complacency and thus deprives the fetus or neonatal infant of the care and attention that might otherwise assure its constitutional adequacy at the time of birth. The percentage of poor results in the delivery of 50 to 100 cases a year does not give the obstetrician a full realization of the similar tragedies involved in 86,000 deliveries, such as those in Massachusetts in 1943. Anoxia is not a matter of percentage or statistics but rather of care and attention that result only from comprehension of the problem. The first question that one may justifiably ask is how these facts may be applied to clinical obstetrics and what can be done about them. The answer is that the obstetrician's own ingenuity is the limiting factor in listing the cause and effect productive of anoxia. The old adage "an ounce of prevention is worth a pound of cure" is nowhere better illustrated than in the prenatal and transnatal period.

The following discussion is limited to the care of the fetus during labor and to the evaluation and treatment of anoxia caused by failure of respiration after birth.

* * *

In any consideration of the care of the fetus during labor, it is essential to remember that, in general, conservative methods are more valuable than the radical ones and that any procedure that benefits the mother is also best for the fetus. The length of labor is of primary importance, anoxia is most frequent in labors under three and those over

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thirty hours. If a labor extends over thirty hours, it is best terminated spontaneously, in the interest of the fetus, without operative interference. The average full-term fetus withstands without severe anoxia a labor lasting twenty to twenty-four hours, including contractions of forty seconds' duration at intervals of from two to five minutes, the parturient mother meanwhile being supported by fluids, glucose, vitamins and oxygen.

My gratitude and my sympathy go to the nurses who attend the medicated patients throughout labor — along with the boredom they have a great responsibility, not only to the fetus but also to the doctor who entrusts it to their care. The fetal heart should be checked every fifteen minutes during active labor of the first stage, and after every other contraction at the end of this stage and during the second stage. It is only through this extra effort on the part of the nurse that the four or five cases in a hundred that would otherwise be lost have an opportunity for salvage. Fetal heart rates of 116 to 160 are in the accepted range of normal. Any deviation from these arbitrary figures should receive immediate treatment by the administration of pure oxygen to the mother, the nurse is the only one in a position to do this in the emergency that may occur at any time during labor. The oxygen is transported directly to the fetus, and its results — in the restoration of a strong fetal heart at a physiologic rate — are as startling as they are reassuring in the vast majority of cases.

The crowning blow to the fetus, battered by hours of labor, is the administration of anesthesia at the time of birth, which results, in many cases, in serious anoxia. For spontaneous or outlet forceps delivery, especially in the face of previous medication, the amount of anesthesia used to complete labor should be absolutely minimal, being sufficient only to dull the pain sense of the mother, or, to use a phrase, sufficient only "to keep her in the room." Nitrous oxide and oxygen should be used in concentrations of 50 per cent each, with a few short inhalations of ether when this is not sufficient. With the head crowning, pure oxygen should be administered to the mother and continued after birth until pulsation of the cord ceases. In operative deliveries — that is, any delivery more serious than outlet forceps — spinal anesthesia is best from the standpoint of anoxia neonatorum (obstructively, version and extraction contraindicate its use because of the continuance of uterine contractions under spinal anesthesia). With spinal anesthesia the mother and infant receive the benefits of pure oxygen inhalation during the entire operative procedure. This advice is given not without a word of caution: the spinal anesthetic should be administered by a competent anesthetist, qualified to treat all its complications, which are more frequent in the pregnant woman, and in a dosage sufficient to

give only relaxation of the perineal soft parts, a so-called "saddle anesthesia."

The greatest single factor contributing to anoxia neonatorum and complicating approximately half the 4 to 5 per cent of neonatal deaths is failure of the onset of respiration after birth. It is essential to have a standard of normal so that deviations from the accepted physiologic response of the respiratory system at birth can be immediately recognized and treated. Respirations should be established within thirty seconds of birth and accompanied by a vigorous cry. The newborn infant should have muscle tone — its absence indicates a dangerous state of anoxia requiring immediate treatment. In the normal infant the time spent in suspending the baby head down and milking the trachea upward toward the mouth to express mucus and debris, as well as the tactile stimulus of brisk rubbing of both sides of the thoracic cage, should initiate the onset of normal respiration. Failure at this point indicates an underlying anoxia, and its severity is best judged by the classification of Flagg,⁴ who determines three stages — depression, spasticity and flaccidity, occurring in that order of frequency and severity.

In the first stage, namely, that of depression, the infant does not breathe well and there is a tendency to dusky skin and recurring cyanosis. Muscular tone is good, and the cord pulsates strongly. Respirations may be free but are slow and irregular. In the treatment of this stage, the infant should be placed in a slightly inclined position with the head downward to promote postural drainage and the mouth and pharynx cleared of mucus and debris by suction, with either a rubber ear syringe or a soft catheter. Body heat should be maintained, preferably by a warm, sterile blanket. Pure oxygen should be administered until the skin shows a pink glow, indicating sufficient oxygenation. If after this stage is reached the baby does not become vigorous, with deep respirations and a cry, it is worth while to stimulate it further with carbon dioxide, and this may readily be done by mouth to mouth insufflation. This will give the infant 5 per cent carbon dioxide, which is regarded by physiologists as a stimulus to the respiratory center. A most important point to remember in the administration of gases to the newborn, is that the lower jaw must not be depressed, for to do so produces an artificial respiratory obstruction. The proper position for the head is slight hyperextension, cradled in the fingers of the hand of the operator and with the thumb forcibly supporting the lower jaw upward. In most cases the procedures mentioned above will ensure the onset of adequate oxygenation and efficient respiration.

The second stage is one of spasticity and is more serious in degree. Respirations, which are irregular, gasping or shallow, occur at long intervals. Reflex

action, such as movement of the facial muscles and extremities in response to suction of the pharynx, is still present. Muscle tone is present but diminished in degree. There is marked cyanosis of the mucous membranes, with blotching of the skin or generalized pallor. Froth or fluid is present in the mouth. The circulatory system is intact, as indicated by the pulsating cord. In the treatment of this stage, the general measures described above are carried out—that is, maintenance of heat, proper position and suction of the upper air passages. It is essential to maintain body heat, and in the absence of warm blankets, the infant should be immersed in a tub of warm water to the neck line. Oxygen should be administered, preferably by a positive-and-negative-pressure machine, which should be regulated to thirty or forty discharges a minute. The machine should be used until the skin becomes pink and the respirations regular—if the machine is employed further at this point the infant's physiologic efforts to set up a respiratory rhythm of its own will be interfered with, a shift should be made to a straight flow of oxygen without alternating positive and negative pressures. In the event that the baby remains pink but does not increase its depth of respiration or cry, 5 per cent carbon dioxide should be resorted to for its stimulating effect. In the absence of a resuscitator, mouth-to-mouth breathing should be initiated at once and maintained until spontaneous respiration is established. In mouth-to-mouth insufflation the proper technic is to cover the nostrils of the infant and to fit the operator's mouth over that of the infant, with a few layers of gauze separating the two. The mouth is filled with air, and the glottis is closed, pressure is applied only by the operator's cheeks. For further protection against rupturing the alveoli during this procedure, the operator's hand should be placed over the thoracic cage of the infant, and there should be only a minimal excursion of the chest wall with each breath blown. Failure to observe these precautions may result in serious damage to the alveoli of the infant's lungs. The mortality and morbidity in this stage are about four times those in simple depression.

The third stage is one of flaccidity and indicates a most precarious state of shock, with circulatory failure, which occurs in about 15 per cent of all such cases and accounts for 75 per cent of all such deaths. Respirations at this stage occur at long intervals or cannot be demonstrated. Pallor or a gray cyanosis is present, and there is a complete

lack of all muscle tone. The apex beat may or may not be demonstrable, and there is no pulsation in the umbilical cord. In these infants, owing to complete lack of tone, there is respiratory obstruction from juxtaposition of the tongue, soft palate and pharynx. In treatment, which should be instituted at once, the general measures discussed above should be carried out, with the important addition of intubation, at first with suction and then with insufflation of gases as outlined in the discussion of the previous stages. Intubation may be indirect, with a catheter, or direct, by use of a laryngoscope, depending on the experience of the operator and the equipment available. The latter is preferable but both methods are adequate. Without intubation, it is impossible to give the infant an adequate supply of oxygen before irreparable damage has occurred to the nervous system.

The administration of drugs to stimulate the respiratory system in these cases is at best debatable, that their use is not without danger is indicated by the fact that in the presence of anoxia they have no effect but that soon after anoxia is relieved by other measures, the stored stimulus may be so powerful as to cause convulsions, with resultant further cerebral damage.

* * *

It is vital to remember that the newborn baby who does not breathe normally is either in or close to a condition of shock and that the utmost gentleness is mandatory, along with the conservation of body heat. The airways must be cleared immediately and completely. It is best to start with pure oxygen to combat anoxia and shock and when this is accomplished, if a satisfactory respiratory response has not been made, to shift to 5 per cent carbon dioxide in an attempt to stimulate the respiratory center. All infants requiring treatment for anoxia should be given the same meticulous care and attention accorded premature infants and should be placed in an incubator at a temperature of approximately 90°F with continuous oxygen for six to twelve hours, being at all times under careful observation.

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DEATH FOLLOWING EXPOSURE TO DDT

Report of a Case

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Numerous authors¹⁻³ have described the toxic effects observed in different species of warm-blooded animals exposed to DDT—2,2 bis (p-chlorophenyl)-1,1,1-trichloroethane—in various ways. By and large, clinical⁴ and pathological⁵ studies of these animals revealed that the principal action of DDT was on the central nervous system and liver.

The general consensus is that, used with reasonable care, preparations containing DDT do not present significant toxic hazards to human beings. Case,⁶ however, reported toxic effects of a 2 per cent solution of DDT on 2 men exposed for forty-eight hours under special conditions, consisting of an oily surface, large areas of skin exposed, high temperature and relative humidity. These effects included an increased destruction of erythrocytes, a decrease in the mean corpuscular content of hemoglobin, an increase in reticulocytes, a diminution of polymorphonuclear leukocytes accompanied by the appearance of immature white cells and the appearance of indoxyl sulfate in the urine. The symptoms and signs included tiredness, heaviness and aching in the limbs, diminution of some reflexes, unilateral slight impairment of hearing, transient yellow vision (in 1 subject), muscular fibrillation (in 1 subject), peripheral patchy anesthesia (in 1 subject), weakness of the legs and a curious apprehensive state. A return to normal took between twenty-six and thirty-three days.

Wigglesworth⁷ mentioned the case of a laboratory worker who allowed small quantities of an acetone solution of DDT to evaporate on the back of his hand. In the course of these experiments, a solution of acetone containing 25 gm of DDT was added to an inert dust and the mixture was kneaded with the hands for some minutes. Three weeks later, the patient was forced to go to bed because of continuous aching in the limbs, sleeplessness and acute anxiety. Involuntary muscle tremors also developed. Recovery was gradual and was not complete at the end of a year.

Hill and Robinson⁸ reported fatal poisoning in a child who drank an ounce of liquid from a bottle containing 5 per cent DDT in kerosene, the dose was approximately 150 mg per kilogram of body weight of commercially pure DDT. Within ten minutes, the child began to cough and vomit. An hour and a half later, convulsions and coma ap-

peared. Death took place four hours after the solution had been drunk. Autopsy showed minimal and indefinite changes in the lungs, liver and spleen.

The purpose of this paper is to report an additional fatal case following exposure to DDT, together with the findings at autopsy.

CASE REPORT

C. C., a 47-year-old, automobile electrician, was admitted to the Massachusetts General Hospital on December 12, 1945, with the complaint of weakness, loss of weight, dermatitis and asthma. Prior to this illness, he had enjoyed good health. No history could be obtained of eczema, asthma, hay fever or migraine in either the patient or his family. On November 10, he had been exposed while at work to a 6 per cent solution of DDT in kerosene. A few hours before he reported to work on that day, the room where he worked with eight other men, measuring approximately 36 x 20 x 10 feet, had been sprayed with the solution. Later in the same day, the patient had resprayed his corner of the room with the contents of the same bottle.† He was conscious of having inhaled the fumes and of contact of his perspiring skin with the solution. He had noted no untoward symptoms until the following morning, when an extensive pruritic eruption had appeared on the trunk and extremities, but had spared the skin of the face. He had also complained at that time of dyspnea and an unproductive cough. During the 5 weeks prior to admission, the cough and dyspnea had become severer. The eruption, which had regressed a few days after the onset, reappeared 1 week later. The patient had remained ambulatory until several weeks before admission, when he had gone to bed because of increasing weakness and a loss of 20 pounds.

During the interval prior to admission, the only medication administered by the patient's attending physician was adrenalin in a strength of 1:1000 given subcutaneously on several occasions. On December 12, one of us (W. R. H.) was consulted and advised hospitalization.

Physical examination revealed an acutely ill and dyspneic man, with a paroxysmal, unproductive cough. The mental status was one of agitation and apprehension. Over the entire cutaneous surface, with the exception of the face, there were numerous discrete, reddish-purple maculopapules varying in size from 2 to 8 mm. Many of these lesions presented an excoriated surface. On one lower extremity, the lesions were hemorrhagic. An ecchymotic area, the size of a twenty-five-cent piece, was noted on the glans penis. The pharynx was dusky red. The tongue was covered with a dry, brownish membrane, and the lips had hemorrhagic crusts. The thorax was emphysematous and hyper-resonant to percussion, with coarse respiratory rales throughout both pulmonary fields. Loud, musical rhonchi were also heard. To percussion, the heart was normal in size. The sounds were of good quality. There were no murmurs. A blood pressure of 110/70 was obtained. The temperature was 98°F, the pulse 120, and the respirations 30. The abdomen was moderately distended, but there was no tenderness or spasm. The liver and spleen could not be palpated. Small, nontender, pea-sized, anterior cervical and inguinal lymph nodes were palpable bilaterally. There were no discernible neurologic signs. A presumptive diagnosis of periarteritis nodosa was made.

Laboratory examination of voided urine revealed an acid reaction, a trace of albumin and no sugar, on microscopic

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‡According to Dr. Hervey B. Elkins, chemist in the Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, 130 cc of 6 per cent DDT had been sprayed on these two occasions into a room with a capacity of roughly 8000 cubic feet. If the spray had been uniformly distributed and none had adhered to the walls, a concentration of 20 to 30 mg of DDT per cubic meter of air would have resulted.

examination there were 15 erythrocytes, 5 leukocytes and rare granular casts per high-power field. Examination of the blood showed a hemoglobin of 12.2 gm (photoelectric-cell technic) and a white-cell count of 43,000, with 72 per cent neutrophils, 1 per cent lymphocytes, 2 per cent monocytes, 20 per cent eosinophils and 5 per cent blast cells, the erythrocytes showed moderate achromia, and the platelets were normal. The sedimentation rate was normal—8 mm in 60 minutes (Westgren). Roentgenographic examination of the thorax showed prominence of the lung roots, with enlargement of the hilar lymph nodes, and going out into each pulmonary field from the enlarged nodes were ragged, linear regions of increased density that extended to the periphery. These findings were reported as consistent with periarthritis nodosa. Chemical studies of the blood, including the serum protein, nonprotein nitrogen, serum phosphorus, alkaline phosphate and carbon dioxide combining power gave normal results. An electrocardiogram was normal except for sinus tachycardia. Repeated blood cultures showed no growth.

A week before death, examination of the urine for organic chlorides, which are said to be increased following DDT ingestion,⁴ was performed, with negative results. (In this case too much time had probably elapsed for the test to be of value.)

On the 2nd hospital day, after the temperature had risen to 103.5°F, 40,000 units of penicillin were administered every 3 hours, night and day. This was continued throughout the hospital stay but had no influence on the temperature, which fluctuated between 102 and 104°F, or on the course of the illness.

On the following day, because of increasing respiratory distress, the patient was placed in an oxygen tent. A few hours afterward, he complained of numbness of the left side of the face and of the index and middle fingers of the left hand. Examination revealed no motor or sensory dysfunction at these sites. The involved fingers were quite cyanotic. The paresthesia disappeared from the face in 12 hours but persisted in the fingers for several days.

On December 15 the edge of the liver was palpated three fingerbreadths beneath the costal margin and was sharp but not tender to palpation. A cephalin-flocculation test was reported to be + + + +. The white-cell count was 40,000, with 61 per cent neutrophils, 10 per cent lymphocytes, 4 per cent monocytes and 25 per cent eosinophils.

On December 18 the patient became slightly confused, and fine tremors of the hands and face developed during movement. The pupils were irregular but reacted fairly well to light and accommodation. Ophthalmoscopic examination showed blurring of the disk margins, as well as distention and tortuosity of the retinal veins. A lumbar puncture, performed 3 days later, showed an initial pressure equivalent to 350 mm of water, the fluid was colorless, and the total protein normal. On December 28 the red-cell count was 3,070,000, with a hemoglobin of 9.5 gm. Specimens removed for biopsy from cutaneous lesions of the left arm and leg, as well as from the muscle of the left lower leg, were reported as showing periarthritis nodosa of both the skin and muscle.

The patient's condition continued to become progressively worse. He became weaker, emaciated and drowsy. The chief complaint at that time was dysphagia. Superficial erosions, covered with a grayish exudate, appeared on the lateral and posterior pharyngeal walls. Because of inability to take nourishment by mouth, the patient was given 1500 cc of saline intravenously each day, together with 1500 cc of 10 per cent glucose mixed with 500 cc of 10 per cent Amigen, 2 cc of Betalin Compound and 100 mg of Cevalin. Transfusions with 500 cc of whole blood were given on January 2 and January 4. On January 6, the temperature rose to 105°F, the pulse to 145, and the respirations to 35. The breathing became more labored, and moist rales were heard throughout both pulmonary fields. The patient failed to respond to therapy and expired at 6:30 a.m.

Autopsy. At post-mortem examination, performed 4½ hours after death, there were purplish petechiae scattered over the serosa and mucosa of the small bowel down to the midportion of the ileum. Peyer's patches and lymphoid follicles were prominent and purplish gray. In the large bowel, there were also a few scattered petechiae. The combined weight of the lungs was 2350 gm. The pulmonary tissue was heavy, boggy and somewhat nodular and firm, particularly in the lower portion of the right upper lobe. The

parenchyma was reddish, with scattered firm, gray and dark-red granular regions measuring up to 2 cm in diameter. The left lung was similar to the right and had regions of gray consolidation scattered throughout. The cavities of the heart were of normal size, and the valves were normal. The liver weighed 2080 gm. The capsule was smooth and transmitted the reddish-brown color of the parenchyma. On section, lobulation was prominent, with large, purplish central regions. The hepatic artery and vein were normal. The kidneys weighed 200 gm each. The capsule stripped readily and revealed a smooth, pale, purplish surface with scattered dark blotches measuring up to 2 cm in diameter. On section, there were dark-purple regions extending radially into the cortex. Elsewhere, the parenchyma was grayish purple and showed regular striations. The glomeruli were pale and bloodless. There were a few dark-red petechiae in the mucosa. The renal vessels were normal. The brain was grossly normal. The right ethmoid and sphenoid sinuses contained a moderate amount of thick, yellowish, purulent material. The upper cervical segment of the spinal cord was not remarkable. The sciatic nerves and the brachial plexus were grossly normal. The brain section after fixation was normal.

Microscopic examination of the lungs showed diffuse bronchopneumonia, with a tendency toward abscess formation in areas of both lungs. The exudate was mainly fibrinopurulent, but erythrocytes and macrophages were frequent. The bronchioles were heavily infiltrated by mononuclear cells and lymphocytes, and some of the thickened walls appeared to consist almost entirely of loose granulation tissue indicating a chronic inflammatory process. The epithelial lining showed various stages of desquamation, and purulent exudate was found in the lumens. Surrounding the bronchioles the pneumonic process was somewhat older than elsewhere, with cuboidal metaplasia of the epithelium in some alveoli and occasional plugs of fibrin infiltrated by large mononuclear cells.

The splenic tissue showed a pathologic process that had been active for a period of weeks or months. The most definite changes were in the corpuscles, which showed a considerable increase in collagen and a decrease in lymphocytes. Plasma and mononuclear cells were abundant, some appearing immature with deeply basophilic cytoplasm. Granules of hemosiderin were frequent both outside and within phagocytes. The red pulp also had a dearth of lymphocytes and appeared congested. Some of the trabeculae were infiltrated by lymphocytes and mononuclear cells. In one section, there was a small infarct with an outer zone of organization and a necrotic center. One of the arterioles contained a fibrin thrombus beginning to undergo fibroblastic invasion.

The central regions of the liver were congested, and there was a moderate fatty change in the periportal regions. One of the large veins contained a fibrin thrombus that bulged out into the lumen and was already covered by endothelium and invaded by fibroblasts.

Some cortical cells of the adrenal glands were necrotic and scattered rounded spaces in the fasciculate cords appeared as if entire cells had dropped out of place.

In the kidneys there were scattered infarct-like regions of parenchymal atrophy and regeneration. The changes were most marked in the tubules, which were small and appeared compressed by the increased amount of vascular connective-tissue stroma. Most of the tubular epithelium was hyperchromatic, as if recently regenerated, but in places the cells were pale and granular, with pyknotic and fragmented nuclei. There were also a moderate number of hyaline casts and a small amount of interstitial infiltration by lymphocytes, mononuclear cells and occasional polymorphonuclear leukocytes. One of the large veins near the hilus contained a thrombus in the process of early organization.

Unquestionably, many persons exposed to DDT will subsequently experience the development of an undiagnosable disease, which will be incorrectly accredited to DDT. In spite of the fact that Neal and Von Oettingen⁹ stated that there is no definite evidence that DDT exerts a sensitizing effect on the skin or produces other allergic reactions, such as asthma, and although, in the case reported above, the exact cause of death could not be determined

at autopsy, it is believed that true allergy to DDT was exhibited and that death was attributable to sensitization by this drug. It is also fair to state that the authors referred to did not observe toxic symptoms in any animals that were exposed to an atmosphere containing many times the recommended insecticidal concentration of DDT when used as an aerosol, mist or spray.⁹

It seems to be more than coincidence for a man who, so far as could be determined, had enjoyed previous good health to experience symptoms twenty-four hours after his first exposure to DDT, and to show subsequently a classic clinical picture supported by laboratory evidence, including blood, urine, biopsy and roentgenographic findings, of periarteritis nodosa. Rich¹⁰⁻¹² and Rich and Gregory¹³ showed that a similar clinical and laboratory picture occurred in persons who had been exposed to sensitizing drugs, such as iodides and sulfonamides, and have claimed that periarteritis nodosa is a hypersensitive state induced by these drugs. It is reasonable, therefore, to assume that DDT also possesses these allergenic properties and should be included among the drugs capable of producing a sensitizing reaction manifested clinically by a picture simulating that of periarteritis nodosa.

The fact that the patient exhibited tremors, a confused mental state, paresthesia and severe loss of weight, symptoms reported both in animals and in human beings as being directly related to DDT intoxication, strengthens the relation of DDT to the final illness.

Even though this is an isolated case, we consider ourselves justified in calling the attention of the medical profession to it, in the hope that it will encourage others to be on the lookout for similar reactions, which, if they occur, will lend support to our assumption.

SUMMARY

A case in which death occurred twenty-five days following exposure to DDT—2,2 bis(p-chlorophenyl)-1,1,1-trichloroethane—is reported. The symptoms, which began in a previously healthy man within twenty-four hours after exposure, were similar to those already reported as due to DDT intoxication. The disease picture, both clinically and at biopsy, simulated that of periarteritis nodosa, and it is assumed that DDT possesses allergenic properties and should be included among other drugs that are believed to be capable of producing such a sensitizing reaction.

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MEDICAL PROGRESS

DIAGNOSIS AND TREATMENT OF SKIN MANIFESTATIONS OF CAPILLARY FRAGILITY*

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THIS subject is discussed under the following headings: vascular anatomy of the skin, with special reference to the site of capillary reactions, the methods of testing capillary fragility, the mechanisms of capillary fragility, the clinical manifestations of capillary fragility as part of general diseases and as purely dermatologic conditions, the relation of capillary-fragility tests to clinical diagnosis, and treatment.

VASCULAR ANATOMY OF THE SKIN, WITH SPECIAL REFERENCE TO THE SITE OF CAPILLARY REACTIONS

The skin is supplied from the underlying tissues through small arteries. In the deepest portion of the cutis the arteries form a rich anastomosing plexus from which small arteries rise perpendicularly to form a subpapillary plexus from which smaller vessels supply the papillary capillaries. These do not anastomose, but each supplies a small but variable number of papillae. Each papilla is normally furnished by a central capillary loop, whose arterial branch is narrow and widens toward the tip to the subsequent venous branch, which may be 0.02 mm or more in diameter. The venous branches of the papillary capillaries then continue to form venules, which return first to a subpapillary plexus of veins. These are connected by short anastomoses with a second venous plexus, which lies at the arterial subpapillary vessels. Between the cutis and the subcutis, valves appear in the veins. No valves are seen in the venules of the cutis.

There is no sharp distinction between the smallest capillary arteries,¹ the capillaries proper and the venules (capillary veins). Lewis² introduces the term "minute vessels" of the skin to distinguish the aforementioned vessels from the "strong arterioles" and the "deep veins."³

Chambers and Zweifach⁴ recently studied the topography and function of the capillary circulation on the mesentery of the rat and dog. The fundamental architecture and physiologic activity of the capillary bed in the mesoappendix of the rat and

in the omentum of the dog were found to be identical in both tissues. No such studies have been made in the capillary bed in human skin. According to these authors, a precise mechanism exists for controlling the rate and the amount of blood flow through the capillary bed. In conclusion, they present the following description:

Muscular elements are present in the capillary bed proper but, instead of being indiscriminately distributed, as indicated by Krogh and his supporters, they are restricted to the well-defined, capillary-like, central channels and their precapillary offshoots. The channels serve as thoroughfares from arteriole to venule and, in this sense, may be regarded as similar to the arteriovenous anastomoses. Functionally, however, they serve a different purpose. They are relatively long vessels and bear a close relationship to the true capillaries. Under normal conditions the central channels always remain open so that any spontaneous restriction of flow is caused by contraction of the precapillary offshoots only.

The recurrent vasomotion of the metarterioles is the factor which controls the rate of flow through the central channels, while the alternate opening and closing of the sphincters of their precapillary offshoots induce an intermittent flow through the true capillaries without interfering with the flow in the central channels. Even during the intervals when their supply of blood is shut off, the capillaries generally contain a fluid. This fluid doubtless diffusing in from the interstitial spaces, is carried by way of the post-capillaries into the distal segments of the central channels and the venules.

A significant feature of the muscular components of the capillary bed, particularly the metarterioles and precapillaries, is their reactivity to epinephrine and to nerve stimuli and their susceptibility to local changes in the condition of the tissue in which they lie. When the tissue is in a state of comparative rest the periodic phases of vasomotion are augmented. This results in a restriction of the circulation to the central channels except for a sporadic blood flow in the true capillaries. Resting tissue is thus relatively ischemic. When the tissue is activated, as by mechanical irritation, so that conditions arising from the tissue predominate, the vasomotion ceases and the metarterioles and precapillary sphincters become dilated. Thereupon, the capillaries become flooded with blood and hyperemia results. The metarterioles and precapillaries form an integral part of the capillary bed proper and their reactive muscular elements are so disposed as to be fully exposed to chemical changes in the environment.

Chambers and Zweifach believe that in the visceral tissues there is the functional autonomy of the peripheral vascular system. An evaluation of the reactions of the capillary circulation has been made possible by their finding that the capillary bed possesses a peculiar architecture with a highly specific responsiveness of its muscular vessels. The most reactive structures are the metarterioles, with their dispersed muscle cells, and the sphincters of the precapillaries. These readily undergo constrict-

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tion through nervous impulses and, conversely, undergo dilation by a-refractoriness to nerve impulses when metabolic waste products accumulate about them. Thus, local tissue conditions can affect the responsiveness of the vasomotion, counteracting the effectiveness of the vasoconstriction.⁵ It will be of interest to learn whether, or to what degree, the findings of Chambers and Zweifach coincide with the vascular anatomy and function of the human skin.

METHODS OF TESTING CAPILLARY FRAGILITY

No exact method is available for the evaluation of capillary resistance. Thus far, methods have been too general and subject to too many variables. Two methods of approach were followed mainly during the last twenty-five years to determine capillary strength. Both depended on the production of skin hemorrhages presumably due to rupture of capillary walls. The suction or negative-pressure test introduced by Hecht⁶ measures the amount of partial vacuum that must be applied to the skin to produce petechial hemorrhage. The original apparatus of Hecht has been modified by a number of workers. Da Silva-Mello⁷ constructed the so-called "capillary resistometer." A similar device was developed by von Borbély⁸ and applied in studies on vitamin P by Szent-Györgyi and his associates.⁹ The other procedure is based on the Rumpel-Leede test, which depends on a quantitative approach by modifications of several authors. It consists in increasing the intracapillary pressure to the point where petechiae appear in the skin. This method was introduced in this country by Hess and Fish¹⁰ and named the "capillary-resistance test." Stephan¹¹ introduced the term "endothelial symptom" and claimed that a positive test signifies a pathologic condition of the endothelial cells of the whole capillary system. The procedure of Göthlin¹² measures the amount of pressure necessary to produce the petechiae. Direct microscopic observation of the affected vessel was introduced by Cutter and Marquardt.¹³ These authors observed the end of the nail bed. The finger of the subject was inserted into a glass holder attached to a negative-pressure apparatus. About half the cases showed the rupture point by petechiae, in the remainder it was assumed that a gap in the capillary line not previously noted meant that rupture had occurred. The authors were unable to produce capillary damage in 14 of about 200 cases.

Koch¹⁴ introduced the so-called "puncture test," in which the skin is lightly pricked with a fine needle. If, on the following day, fine bleeding points are visible at the sites of the puncture, it is claimed that the patient shows a bleeding tendency. This test was later applied by Hess,¹⁵ who punctured the skin by a hypodermic needle and observed whether a hemorrhage resulted. He also observed whether numerous subcutaneous injec-

tions of diphtheria antitoxin in a case of diphtheria resulted in hemorrhage but found not the slightest extravasation at the site of injection.

Leschke¹⁶ used the puncture test as a starting point for his bleeding test. He injected subcutaneously 1 or 2 cc of a 0.2 per cent sodium chloride solution. He claimed that this saline concentration produced a stronger irritation than physiologic saline solution. In a patient with a bleeding tendency he found a subcutaneous hematoma, this was a case of thrombocytopenic purpura.

A better controlled skin test is that introduced by Peck, Rosenthal and Erf,³ which employs snake venom. The venoms of various species of snakes differ in their content of toxic principles, such as hemorrhagins, blood coagulants, hemolysins and neurotoxins. A method for the demonstration of hemorrhagins in snake venom has been devised by Witebsky, Peck and Neter.¹⁷ The venom used is that of the moccasin (*Agkistrodon piscivorus*). The venom is titrated by observation of the effect on the vascular bed of the chick embryo. The optimum dilution of venom in 1 cc of physiologic saline solution is that which produces petechial hemorrhages in the four-day chick embryo in a three-hour period. This is considered to contain 10 hemorrhagin units. Thus, 0.1 cc of standardized venom contains 1 hemorrhagin unit.

The intradermal venom test consists in the intradermal injection of 0.1 to 0.2 cc (1 or 2 hemorrhagin units) of standardized moccasin venom, the reaction being determined within thirty minutes to an hour. A solution of 0.1 to 0.2 cc. of physiologic saline injected at the same time served as a control. The test is positive when a definite capillary rupture or ecchymosis appears at the injection site within an hour. The ecchymosis may be 1 cm or more in diameter. A delayed positive reaction is one that shows a diffuse ecchymosis in twelve to twenty-four hours. A negative test is one that demonstrates no hemorrhagic discoloration of the skin.

The venom reaction can be used to determine local capillary fragility. Areas can also be used that are inaccessible to the tourniquet test, such as the cheek, the mucous membranes and the center or periphery of skin lesions.

The test appears to give valuable information in thrombocytopenic purpura hemorrhagica, both in the classification of such cases and in the prognosis. It was positive in symptomatic purpura associated with benzol poisoning, aplastic anemia, leukemia, subacute endocarditis and so forth. Although the purpura in those cases was closely related to the platelets, the test did not necessarily serve as an indicator of the platelet count alone. The venom test gave varying reactions in different types of purpura not associated with a diminution of the platelets.¹⁷ The mechanism of this action is not yet understood.

MECHANISMS OF CAPILLARY FRAGILITY

Bleeding or hemorrhage originates if whole blood escapes from a blood vessel. This phenomenon occurs from a variety of causes, some of which are known, whereas others remain obscure. Extravasation of blood is always due to a separation in the continuity of the blood vessel, which can be brought about by three major processes: rupture of a blood vessel, corrosive or ulcerative perforation of a blood vessel, and diapedesis through the unruptured, nonperforated wall of a blood vessel.

The first group usually comprises hemorrhage from simple and obvious causes, such as open injury and blunt, contusive and tearing forces. Rupture following formation of aneurysm or local dilatation of the lumen with a thinning wall may be taken as a pathologic process in this group. One may speculate that hyaluronidase affects the permeability of blood capillaries, as originally emphasized by Meyer and Chaffee.¹⁸ These authors explain the occurrence of hyaluronic acid in skin as an indication for the identity of the spreading factor and hyaluronidase in the so-called "spreading or diffusion reaction."^{19, 20} On the hypothesis that the capillaries and minute vessels are surrounded by a tissue containing hyaluronic acid, capillary permeability may be due to hyaluronidase activity that liquefies the surrounding tissue, with the result that the walls of the minute vessels are no longer adequately supported. The intravascular pressure then dilates the vessels to such a degree as to rupture them. In preliminary unpublished experiments with a certain bacterial toxin by Chambers and Zweifach,²¹ this possibility was experimentally corroborated.

The histologic studies of both clinical and experimentally produced purpuric lesions by Peck, Rosenthal and Erf² suggested that the tissues surrounding the minute vessels, especially the elastic fibers, play an important role in hemorrhage from blood-vessel rupture. The chief basis for their conception was the histologic studies of skin biopsies from patients with Schönlein-Henoch's purpura at various stages of the disease. In the active stages a toxic effect on the vessel wall was evidenced by purpuric manifestations all over the body, and the venom test then was positive, although somewhat different in type in all areas of the skin. When recovery occurred, the venom tests became negative in all areas of the skin. During convalescence and for some time thereafter, when the patient had become ambulatory, purpuric manifestations often occurred only on the lower extremities. The venom test was still negative throughout, even on the lower extremities, suction tests were sometimes positive on the lower extremities in such patients. In the ambulatory cases, histologic examination of skin biopsies from the lower extremities apparently showed changes in the elastic tissue, especially

around many of the small vessels. The vessels themselves seemed normal. These findings were interpreted as demonstrating that although the capillary vessels themselves had returned to normal, the loss of the cushioning effect resulting from the damage to the elastic tissue immediately surrounding the vessels gave rise to purpuric manifestations when there was an increased intracapillary pressure, as in walking. The venom test was negative in such cases because the vessels themselves had apparently returned to normal. On the other hand, tests like the suction tests were positive because petechiae produced by such a method also resulted when the resistance of the supporting structures immediately around the vessels was nullified.

Hemorrhage from perforation of blood vessels includes those due to burns and corrosive agents, as well as those due to various pathologic processes, as in gastrointestinal ulcers, in cerebral hemorrhage and generally in arteriosclerosis caused by a patch of atheroma and its corrosive action. It should be emphasized, however, that cerebral hemorrhage is also caused by arterial thrombosis or embolism. Under such conditions, attempts to accelerate blood clotting may serve to aggravate the bleeding. In typhoid fever and subacute bacterial endocarditis, for example, clumps of bacteria or platelet thrombi containing bacteria may lodge as emboli in the capillaries and cause hemorrhage. In the present state of knowledge it does not seem possible to decide whether menstrual bleeding belongs to one of the groups discussed above or to the third group.

Hemorrhage through the unruptured wall of blood vessels comprises conditions in which many small hemorrhages, often of the size of a pinhead, or petechiae, occur. Ecchymoses are apparently based on the same phenomenon and signify larger extravasations. Chambers and Zweifach²¹ made the observation that the interendothelial cement provides considerable cover for the endothelial cells facing the capillary lumen. This cement substance, when removed, permits hemorrhage. Chambers and Zweifach²² believe that the intercellular cement is secreted by the endothelial cells. On this basis, increased capillary fragility leading to extravasation may be due to injury of the cement substance or to inability of the endothelial cells to secrete this substance continually.

In septicemia it has been assumed that bacterial toxins injure the capillary endothelium and produce petechial hemorrhages, mainly in the serous membranes. Hemorrhagic purpuras, particularly, represent characteristics by the formation of purple patches on the skin and mucous membranes that appear to be based on this type of hemorrhage. In telangiectasia or angiomas, multiple localized dilatations of the capillaries and venules, particularly of the skin and mucous membranes, are found. In these hereditary or acquired vascular anomalies, spontaneous bleeding, possibly due to hemorrhage

through either ruptured or unruptured walls of blood vessels, occurs, trauma, however, is frequently the cause of hemorrhage of both types. Thus, in these hemorrhagic disorders bleeding may be brought about by any of the three major processes discussed above.

The above classification of the initial causes of bleeding by the three major processes that separate the continuity of the blood vessel does not suffice, since the phenomenon of bleeding has as a counterpart the phenomenon of hemostasis, which is defined as arrest of hemorrhage.

It is obvious that, because of the difference in the mechanisms of capillary hemorrhage, a single therapeutic approach to secure hemostasis cannot counteract the manifestations of capillary fragility. These phenomena have never been adequately studied, partly because no proper methods have been devised for their study. At present such investigations are being made by Chambers and Copley.²³

CLINICAL MANIFESTATIONS OF CAPILLARY FRAGILITY

General Diseases

Wiemer²⁴ differentiates the following factors that influence capillary resistance: those directly damaging the endothelium, including poisons, such as opium, neoarsphenamine, carbon monoxide, trypaflavine and iodine, toxins, as in scarlet fever, polyarthritus, measles, diphtheria, smallpox and influenza, metabolic products, as in uremia and acetoneuria, and vitamin deficiencies, such as scurvy, and those indirectly affecting the endothelium or capillary tonus, comprising physiologic variations, such as those previous to menstruation and in endocrinal disturbances, endocrine diseases, such as exophthalmic goiter and *climacterium virile*, and diseases of the spleen and the reticuloendothelial system. In addition to the conditions listed by Wiemer, increased permeability of the wall of peripheral vessels has been found in tuberculosis. In tuberculous children with purpura an increased bleeding time and a decreased capillary resistance were observed in association with a normal platelet count, coagulation time and calcium content.²⁵

The pathogenesis of essential thrombocytopenic purpura is poorly understood.²⁶⁻²⁷ Rosenthal²⁷ considered weakness in maturation or fragmentation of megakaryocytes an important factor in the origin of the disease. He briefly reviewed the literature of the disease. He briefly reviewed the literature pertaining to splenic functions that are possibly important in inhibiting thrombocytopoiesis. A similar view was recently expressed by Dameshek and Miller,²⁸ who postulate a hormonal relation between the spleen and the bone marrow and who regard the disease as being due to a form of hypersplenism in which the megakaryocytes of the bone marrow are inhibited from normal platelet production and delivery.

Increased capillary fragility and increased bleeding time correspond to the hemorrhagic tendency. Several workers consider lesions of the vessel walls to be the primary defect in this disease,²⁹⁻³¹ although the actual morphologic evidence of the presence of such lesions is not decisive.

It should be considered that increased capillary fragility as measured with the venom test of Peck, Rosenthal and Erf,³² a negative-pressure or positive-pressure test or with the new technics developed in animals by Chambers and Copley,²³ may not necessarily indicate an increased hemorrhagic tendency. In certain chronic conditions such as arteriosclerosis, hyperthyroidism and diabetes, increased capillary fragility may be present without the clinical picture of a hemorrhagic diathesis.

Dermatologic Conditions

A state of capillary fragility is not infrequent in many dermatologic conditions. Changes in the small vessels are seen, for instance, in such abnormalities as purpura due to drugs, Majocchi's disease, angioma serpiginosum, Schamberg's disease, pigmented purpuric lichenoid dermatitis, Kaposi's disease, Osler's hereditary familial telangiectasia, orthostatic purpura and dermatitis hemostatica.

RELATION OF CAPILLARY-FRAGILITY TESTS TO CLINICAL DIAGNOSIS

Several major processes concerned with hemostasis, either singularly or in some combination, are summarized as follows: clotting of blood due either to fibrin formation and blood coagulation or to platelet agglutination, blood-vessel changes, physical properties of blood clots, and adhesiveness of blood clots or so-called "wound thrombi" to the vessel wall. This classification is fundamentally identical with that of hemorrhagic disorders. It differs from the generally accepted division of bleeding diseases, which only accepts two primary groups—in which the hemostatic defect is vascular, and in which the mechanism of blood coagulation is disturbed. This limited classification of causes of defective hemostasis or hemorrhagic disorder not only omits significant phenomena, such as the physical properties and adhesiveness of blood clots, but also recognizes only one mechanism of blood clotting—namely, blood coagulation. The generally accepted contention is no longer tenable because of a series of findings made by Copley and his associates.³³⁻³⁹

Copley and Houlihan³³ showed that the agglutination of platelets is not brought about by fibrin formation and that the two processes are governed by different mechanisms. Copley and Lalich³⁴ demonstrated that the firmness of the clot and its property of adhesion to the traumatized vessels are probably important in maintaining hemostasis; they expressed the belief that both the agglutination of platelets and the conversion of fibrinogen to fibrin

are responsible for the properties of the clot that seals the wounded vessels. In a subsequent study on the mechanism of hemostasis they³⁵ emphasized that the clot that forms in a wound is similar to or identical with a thrombus and therefore designated such a clot as a "wound thrombus." On the basis of recent studies on platelet agglutination by Copley and Houlihan^{33, 36} and on coagulation thrombosis in arteries and veins of dogs by Copley and Stefko,³⁷ a new concept of the phenomenon of thrombosis was advanced.³⁸ According to this view, either the agglutination of platelets or the formation of fibrin with simultaneous or subsequent blood coagulation, and not necessarily always a combination of both phenomena, forms wound thrombi to effect initial hemostasis.

Few tests were available for studying hemorrhagic disorders. Since some of these procedures were improved by a number of workers and a series of new technics were developed by Copley and his associates, a reclassification of hemorrhagic disorders becomes necessary. The following tests are recommended for clinical study of hemorrhagic conditions in men: blood-saline coagulation time (Copley and Houlihan³⁹), prothrombin time—the one-stage method (Quick⁴⁰) and the two-stage method (Warner et al⁴¹), antithrombin content (Astrup and Darling⁴²), platelet count on both venous (Copley and Robb⁴³⁻⁴⁵) and cutaneous blood (Ottenberg and Rosenthal⁴⁶), platelet agglutination tests—macroscopic (Copley and Houlihan³⁶) and microscopic (Houlihan and Copley⁴⁷), clot-firmness test (Lalich and Copley⁴⁸), thixotropy and dilatancy tests (Copley et al⁴⁹), syneresis or clot retraction (MacFarlane⁵⁰), extracorporeal clot volume (Lucia, Aggeler and Hamlin⁵¹), bleeding time (Copley and Lalich^{34, 52}), clot resistance (Copley and Lalich^{34, 52}), and capillary fragility, including the skin venom test of Peck, Rosenthal and Erf,^{32, 53} the positive-pressure test of Göthlin¹² and the negative-pressure test of Da Silva-Mello⁷ and Cutter and Marquardt.¹³

The first nine tests aid in measuring the hemostatic function of the blood. The physical properties of the blood coagulums are measured by the tests for clot firmness, thixotropy, syneresis and extracorporeal clot volume. The hemostatic function of the skin is measured by the determinations of bleeding time, clot resistance and capillary fragility. The majority of hemorrhagic disorders will have to be restudied with the newer methods. Only then will it be possible to arrive at a proper diagnosis. It is our opinion that such studies not only will advance knowledge on hemorrhagic disorders but also will lead to a more intelligent and adequate therapy. Hemostatic agents are frequently used promiscuously to arrest hemorrhage. Unfortunately, poorly controlled usage of various hemostatic agents is both valueless for a better understanding of hemorrhagic disorders and possibly dangerous to patients.

TREATMENT

Most authors have reported no therapeutic success following the administration of large doses of vitamin C in other than clinical and subclinical scurvy. In a recent publication, Goldman and Corrill⁵⁴ reviewed the therapeutic results obtained with vitamin P; they reported that clinical trials with crude hesperidin and hesperidin methyl chalcone in patients exhibiting obvious capillary fragility were of no value. Transient and at times striking decreases in the positive tests for capillary fragility, however, were occasionally noted after the intravenous use of hesperidin methyl chalcone.

It has been shown in certain cases of thrombocytopenic purpura by Peck, Rosenthal and Erf,⁵⁵ and others^{27, 56} that therapy with moccasin venom was of some value. In a recent review of the classification and treatment of purpuric conditions Rosenthal⁵⁷ stated that nonoperative treatment of thrombocytopenic purpura was apt to be unsatisfactory if cases occurring in children and some acute cases in adults were excluded. Recovery was spontaneous in many idiopathic or infectious cases, especially in those due to drug idiosyncrasy. X-ray irradiation of the spleen, ascorbic acid given intravenously and orally and citrin were unsuccessful in the treatment of chronic purpura. There was no evidence of the value of sesame oil, liver extract or parathyroid extract in the treatment of idiopathic purpura. Blood transfusions were indicated in the presence of severe symptoms, to tide patients over the critical period until splenectomy could be performed. Snake venom, which was of value in the treatment of the nonthrombocytopenic forms of bleeding, hastened recovery in certain cases but was ineffective in acute thrombocytopenic purpura or in the acute forms in which there was a megakaryophthisis. In this group, severe reactions may follow the intracutaneous or subcutaneous injections of snake venom. In chronic cases in which the patients refused to submit to splenectomy, snake venom had some therapeutic value.

Rosenthal⁵⁷ reported on additional patients with chronic purpura treated with venom since the last published report with Peck. Only about 50 per cent of his cases showed symptomatic improvement following its use. His conclusions were as follows:

In no instance have we found a change in the number of blood platelets following the venom injections. In only a few has there been a tendency towards diminution in the bleeding time, but more frequently we have seen improvement in the condition of the capillaries as noted with capillary resistance tests. On the whole we believe snake venom therapy should be regarded only as a palliative form of treatment in this condition. The intracutaneous venom test, however, is of value from the prognostic standpoint, especially in the selection of cases requiring splenectomy. It has been noted that a reversal from a positive to the negative intracutaneous venom test, after repeated inoculations usually was associated with improvement. The persistence of positive intracutaneous tests usually indicates the ineffectiveness of venom treatment, and in a small number of cases, also failure to react to splenectomy.

Splenectomy is undoubtedly the most promising form of treatment and, in the great majority of cases, perhaps the only curative one, according to Rosenthal. He emphasizes the fact, however, that it is essential to weed out acute and apparently chronic cases in which splenectomy is contraindicated, and observes that the intracutaneous venom reaction and sternal puncture were of considerable value for this purpose. Cases with a reversal and most cases with a persistent positive venom reaction do well after splenectomy, in the latter the venom reaction becomes negative after operation. There are cases with persistent positive intracutaneous reactions that do not improve after splenectomy. The appearance of a violent reaction from intracutaneous venom injection, such as an excessive hemorrhagic reaction or the appearance of bullae or exaggeration of the purpuric state, may be regarded as a definite contraindication to operation. Such reactions occur in the severe types of acute purpura mentioned above. Absence or marked diminution in the number of megakaryocytes in the bone marrow is also a definite contraindication to splenectomy.

Schönlein-Henoch's purpura is also known as Frank's hemorrhagic capillary toxicosis or peliosis rheumatica. In this condition there are various degrees of purpuric eruptions on the skin, as well as polyarthritides. Although the treatment is symptomatic, a few cases have apparently responded to moccasin venom. According to Rosenthal, tonsillectomy may be of value in the chronic form.

In the so-called "endocrinal ecchymosis" often seen in women, good results have been obtained in a number of cases with moccasin snake venom. Some patients with Schamberg's disease and Osler's hereditary familial telangiectasia, as well as with Majocchi's disease, have been treated by means of snake-venom injections. In a number of cases there was apparently a good therapeutic result following the injections. In others, especially in Osler's disease, the venom therapy had very little influence on the course of the epistaxis.³³

The clinical use of snake venom has been made on a more or less empiric basis. It is possible that the therapeutic effects of successive small doses given over a long period are due to the development of agents that resisted the destructive action of the toxins. It is also possible that some element in the capillary walls, such as that described by Chambers and Zweifach,⁴ may be so changed that the capillary resistance is affected. So far as thrombocytopenic purpura is concerned, it should be kept in mind that neither the pathogenesis of this disease nor the action of the moccasin venom in decreasing capillary fragility is understood.

The discussion on capillary fragility given above presented the phenomenon as being due to several mechanisms. Hence, the finding that the capillary fragility is counteracted by any one treatment

must be qualified by the specific conditions under which the subject happens to be during such treatment.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

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EDITH E PARRIS, *Assistant Editor*

CASE 32511

PRESENTATION OF CASE

A seventeen-year-old high-school girl entered the hospital because of nervousness, perspiration, weakness and weight loss

Three months before admission she had noted increasing nervousness, profuse perspiration and weakness About a week later, during a pre-employment examination, she had been told that she had high blood pressure and thyroid disease and had been referred for treatment to a hospital, where examination revealed a temperature of 99°F, a pulse of 140 and respirations of 28 The blood pressure was 190 systolic, 140 diastolic, there was dyspnea without cyanosis, as well as a cold moist skin, bilateral exophthalmos with slight lid lag, slight narrowing of the retinal arteries, an enlarged heart and a Grade II apical systolic murmur The skin showed areas of macular eruptions, some of which were pustular and some healing Neurologic examination was negative except for a fine tremor The thyroid gland was not palpable During the ten-day hospital stay 15 drops of Lugol's solution had been given three times a day, but there had been no improvement in the symptoms and the basal metabolic rate, which had been +69 per cent initially, had not been changed The patient had been discharged to the outpatient department At that time attacks of paroxysmal nocturnal dyspnea with severe palpitation and insomnia had appeared A poor appetite rendered her diet inadequate, there had been a weight loss of 6 pounds in two months No history of intolerance to heat, of diarrhea or of

emotional upsets was elicited The eyes were said to have always been prominent During the next four weeks spent at home in bed and for a week after her second hospital admission she had taken 150 mg daily of 6-propyl-thiouracil After a week of treatment signs of left ventricular failure had been more definitely manifest, the patient had been digitalized, with immediate improvement, and had been maintained on 0.1 gm digitalis daily thereafter She had continued to lose weight and was readmitted to the hospital two months before entry to the Massachusetts General Hospital The physical findings had not changed The outstanding laboratory values were a white-cell count ranging between 10,000 and 11,000, with 85 per cent neutrophils, a normal red-cell count, a + test for albumin in the urine, with 1 white cell and 1 red cell per high-power field in the sediment, and a specific gravity consistently between 1.015 and 1.020, a blood cholesterol of 137 and 180 mg, a fasting sugar of 115 mg and a total protein of 6.6 gm per 100 cc and a basal metabolic rate of +79 per cent X-ray films of the skull had been normal, and those of the chest had shown cardiac enlargement and slight congestion of both lung fields An electrocardiogram had shown evidence of left ventricular strain and digitalis effect An intravenous pyelogram had revealed a double right ureter A phenolsulfonephthalein test and a serum nonprotein nitrogen had been normal The hospital course was marked by a low-grade fever and rapid pulse and respirations The blood pressure, taken three times a day and during sleep, had not varied appreciably, ranging between 200 systolic, 140 diastolic, and 190 systolic, 120 diastolic A gallop rhythm and pulsus alternans had developed, but the patient had remained ambulatory without respiratory difficulty Two months later she was referred to this hospital Physical examination revealed that the weight was 99 pounds, the normal having been 140 pounds The patient was calm and did not appear acutely ill The skin rash was still present There were palpable lymph nodes in both groins and a palpable node in the posterior cervical region The heart was enlarged to percussion A Grade II systolic murmur and a diastolic "blow" were audible in the fifth interspace at the left border of the sternum The thyroid gland was not palpable Rectal examination revealed hard fecal material

The temperature was 99°F, the pulse 144, and the respirations 30. The blood pressure was 180 systolic, 120 diastolic, in the left arm and 210 systolic, 150 diastolic, in the right arm.

Examination of the blood showed a red-cell count of 4,200,000, with a hemoglobin of 11.3 gm. The urine persistently showed a + to +++ test for albumin, and the sediment contained a moderate number of casts and 2 to 20 white cells per high-power field. A stool was guaiac negative. X-ray examination of the chest showed the heart to be greatly enlarged. The thyroid region was normal, and no substernal mass was visible. The esophagus was not deviated. One day later a plain film of the abdomen showed barium in the right side of the colon and a large amount of air in the rest of the colon.

An electrocardiogram disclosed a rate of 120, with normal sinus rhythm, the PR interval equaled 0.16 and the QRS complex 0.05 second, with normal voltage. There was a low T₁, a slightly inverted T₂, and an inverted T₃. The blood chloride was 96 milliequiv per liter. The protein, cholesterol, non-protein nitrogen, fasting blood sugar, calcium, phosphorus and alkaline phosphatase were normal. The glucose-tolerance curve (oral) was 93 mg per 100 cc fasting, 154 mg after thirty minutes, 146 mg after sixty minutes and 67 mg after 120 minutes. The corrected sedimentation rate was 0.93 mm per minute. The urea clearance was normal. The basal metabolic rate was +62 per cent.

In the hospital there was a persistent temperature of 99 to 100°F. The pulse and respirations were rapid, and the blood pressure was continuously elevated. The gallop rhythm heard previously was still present, and the neck veins pulsated. The circulation time (arm to tongue) was 15 seconds. The patient was cheerful and subjectively well until the end of the first hospital week, when she had a two-day episode of cramping abdominal pain and constipation without nausea or anorexia. The pain disappeared, but the constipation remained despite enemas and cathartics. Hard, lobular masses were palpated in the midabdomen and left lower quadrant. Proctoscopy revealed no fecal or tumor masses.

On the thirteenth and sixteenth hospital days x-ray films revealed a large amount of barium mixed with intestinal contents obscuring soft-tissue details in the abdomen. There were distention of the lower abdomen and mild paraumbilical tenderness. On the seventeenth day cramping pain again began, and the patient vomited several times. Distention increased, and peristalsis decreased. Additional enemas had no effect. A small amount of barium introduced by rectum showed an obstructing mass in the sigmoid. Its nature could not be determined, although it was thought to represent impacted feces. Some barium escaped around it into the colon. On the eighteenth and nineteenth days the white-cell count rose to 22,600. The temperature remained

at 102°F, the pulse became feeble, and peristaltic sounds disappeared. The blood pressure stayed high. It was decided to perform a cecostomy. At operation the cecum was greatly distended. A tube was inserted after deflation. The patient then began to vomit persistently and expired, apparently after aspiration of vomitus.

DIFFERENTIAL DIAGNOSIS

DR PAUL D. WHITE: When I read this case over, it looked like one for the book. I might add that Dr. Graybiel and I some day hope to publish a volume of unusual cases and rare types of heart disease.

One thinks of infection to account for the symptoms in a patient of this age. Another condition to account for them is thyrotoxicosis. Psychoneurosis is a possibility, but I should put infection and thyrotoxicosis first.

The pulse rate was out of proportion to the other findings except for the blood pressure. The combination of marked tachycardia and marked hypertension is unusual in either thyrotoxicosis or hypertension.

The skin showed areas of macular eruptions, some of which were pustular and some healing. That finding is confusing. Why it occurred, I have no idea. I do not know whether it fits in with my final diagnosis.

There is no statement whether the paroxysmal arrhythmia, auricular fibrillation or paroxysmal tachycardia had persisted. Thus, we have a patient with marked hypertension who could have had acute heart failure even without arrhythmia.

I do not know whether the prominence of the eyes was marked or simply a slight congenital exophthalmos with a slight lid lag. Therapy was evidently aimed at thyrotoxicosis, but left ventricular weakness became manifest, and despite the persisting tachycardia and hypertension, digitalization helped the symptoms of heart failure.

This is a characteristic record, I judge, of a hypertensive heart, without the need for diagnosis of any other kind of heart disease. At first, there was no evidence of renal insufficiency or any serious structural abnormality of the kidney. On admission the patient had lost a great deal of weight—over 40 pounds.

There is no statement regarding the appearance of the skin rash on admission. I suppose that it had the same appearance as previously.

DR TRACY B. MALLORY: Can you describe the rash better, Dr. Beckman? Did it look like acne?

DR WILLIAM BECKMAN: No, it was macular, with flat reddish lesions. It looked somewhat like a phenobarbital rash.

DR WHITE: Was the patient receiving phenobarbital?

DR BECKMAN: No.

DR WHITE: Were the lesions large?

DR BECKMAN I thought that they were definitely abnormal, about 2 cm in diameter

DR WHITE The murmur had not changed There was a diastolic blow, but I judge that it was rather slight Whether it could be attributed to the failure of the aortic valve to hold against such a high pressure as stated, I do not know, but I rather suspect that that is the answer, rather than endocarditis

I assume that there was a good enough pulse in the feet, however Can you answer that, Dr Beckman?

DR BECKMAN Yes, there was

DR WHITE That helps to rule out possible deformity in the aorta, in particular, coarctation, which can be attended by a difference of the blood pressures in the two arms I should also like to know if that blood-pressure difference was noted elsewhere, or before or after this occasion It was probably not a remarkable finding

DR BECKMAN I thought that it was not remarkable I do not remember being impressed by it at all

DR WHITE One does find pressure differences normally in the two arms

If the test is repeated, the blood pressure in the same arm is sometimes different the second time from that on the first occasion I should not pay too much attention to that one observation

Renal involvement was more evident on admission to this hospital

A thoracic goiter—that is, a thyroid tumor in the mediastinum—was being looked for

Was the barium in the colon that which was previously put in for study of the esophagus?

DR BECKMAN So far as I know

DR WHITE The electrocardiogram was not diagnostic, nor was it a remarkable record The T waves could have been low because of tachycardia

We now come to the beginning of the symptoms in the abdomen, where there is indication of some trouble According to the record, there appeared to be an unusual amount of air in the colon

Was new barium given, or were the latest x-ray findings due to the old barium?

DR BECKMAN It was the same barium

DR WHITE It had been in the gastrointestinal tract a long time In other words, there was more and more evidence of intestinal obstruction

In the discussion of the diagnosis, certain things are obviously important clues These include the high basal metabolic rate, which must be taken into consideration, the high blood pressure with cardiac enlargement and failure resulting therefrom and the rapid pulse Much effort was made in an unsuccessful attempt to find a thyroid tumor somewhere The picture, of course, does not fit thyrotoxicosis We do not expect to find hypertension in thyrotoxicosis, although other findings do fit—namely, the tachycardia, high basal metabolic rate,

tremor, exophthalmos and weight loss This patient certainly does not fit the picture of Cushing's disease Except for the hypertension and heart enlargement and failure therefrom, the picture does not fit essential hypertension We must put together the hypertension and the signs that do not go with hypertension as a rule The abdominal symptoms, and signs that appeared toward the end strongly, suggest some degree of intestinal obstruction

I believe that it is possible to fit most of this picture together,—although there are some clues that I am unable to make use of, such as the skin lesions,—if we make a diagnosis of an adrenomedullary cell or chromaffin-tissue tumor, which would be called a pheochromocytoma if located in one of the adrenal glands or a paraganglioma if occurring outside in the sympathetic ganglions Some of these tumors grow to a large size, but I am not familiar with them I have seen little of this disease, although a good many cases have been well described Such tumors may conceivably obstruct the lower gastrointestinal tract, especially if outside the adrenal gland itself The combination of symptoms and signs certainly fits the picture of what might be called the suprarenal sympathetic syndrome tachycardia, hypertension, high basal metabolic rate, weight loss, tremor and so on I cannot explain the skin lesions, however, by this condition I thought of disseminated lupus as an explanation of the skin lesions, but the rest of the case does not back that up

My diagnosis therefore is pheochromocytoma or paraganglioma, probably the latter, leading to marked and malignant hypertension with resulting cardiac enlargement and failure and in some way causing terminal intestinal obstruction In patients with chromaffin-tissue tumors, paroxysmal attacks of hypertension and other symptoms frequently occur, but the hypertension often remains constant

DR OLIVER COPE I should like to add certain information that is not in the record I think it is only fair to place before Dr White some of the complexities that faced the clinical service I saw the patient because she was sent to this hospital with a question of one of the diagnoses that Dr White has made—that is, pheochromocytoma The other hospital had considered and rejected thyrotoxicosis Five days after admission to this hospital the patient developed a pericardial friction rub It was pointed out to me by one of the medical residents, it was clear and distinct Am I correct, Dr Beckman?

DR BECKMAN Yes, it was there

DR COPE It was assumed that pericarditis was present

DR J H MEANS Dr Cope, you are familiar with the pseudopericardial friction rub?

DR. COPE It was not one of the pseudopleuro-pericardial friction rubs heard over the pulmonic area, this pericardial rub was heard over the entire precordium and loudest over the apex impulse. It was not influenced by respiration. We went through that carefully. One physician, however, thought that it was not a pericardial rub.

DR. MEANS It is well known that in moderate thyrotoxicosis a noise can be heard over the heart that sounds like a pericardial friction rub toward the base. We have been familiar with that for years. The thing to remember is that it is of no importance because if the thyroid gland is removed and the thyrotoxicosis cured, the noise disappears. I do not know how it is produced. This patient had a high metabolic rate, and I wonder if the kind of noise you are talking about might not have been of that variety.

DR. WHITE It was probably due to bulging of the artery. A pericardial friction rub can be present without pericarditis.

DR. MEANS Believe it or not, I had written down pheochromocytoma, question mark, before Dr. White mentioned it. I do not know whether that is the correct diagnosis. I had also thought of lymphoma, however. It did not satisfy me, but it had to be thought of. I thought of leukemia, but there was no indication of leukemia.

DR. JOSEPH C. AUB The white-cell count was suggestive.

DR. MEANS I should approach this case as Dr. White did. Because of the similarity of the symptoms to those of thyrotoxicosis, a number of methods for detecting that condition must be used but there is no evidence that they were employed in this case. The blood iodine, for instance, would have been of importance.

DR. BEVERLY TOWERY It was normal.

DR. MEANS If normal, it weighs heavily against thyrotoxicosis. Another method is to observe the uptake of radioactive iodine by the thyroid gland. The hyperplastic gland takes up more than the normal.

DR. RULON W. RAWSON That was done, and the result was within normal limits.

DR. MEANS I agree with Dr. White. The only other test that might have been used is creatine tolerance. I think that thyrotoxicosis can be ruled out, in spite of the marked elevation of the metabolic rate. I wrote down several causes of high metabolic rate. One was thyrotoxicosis, another leukemia, another fever, another a hole in the eardrum, and still another that the patient was apprehensive every time the apparatus was used and that the test was not basal. Another possibility is an abnormal amount of adrenaline. I remember that some years ago, when my metabolic rate was being tested every day for an experiment, it was always normal until one day it was +40 per cent.

The technician asked if I had suddenly developed Graves's disease? I said no. I did not have Graves's disease, but that on the way to the laboratory I had had an alteration, which raised the rate. I apparently had shot myself full of adrenaline in the alteration. I think that it would be reasonable to explain the high metabolism in this case on an excess of the only hormone other than thyroxine that I know of that has a characteristic calorogenic action, namely, adrenaline, which is a quick-acting hormone, whereas thyroxine is a slow-acting one. Adrenaline might be discharged continuously and thus give a sustained high metabolism. A tumor of the medulla of the adrenal gland might cause a continuous output of adrenaline, and I agree entirely with Dr. White that that is probably the diagnosis in this case. I cannot see any other diagnosis that could fit this combination of hypertension and hypermetabolism in the absence of thyrotoxicosis. If there is something else, it has not entered my field of consciousness.

One other point about a pheochromocytoma: we used to be taught that the characteristic picture was a series of seizures or hypertensive crises in which the patient might die, but that between these seizures the blood pressure was normal. Dr. White has told us that that is not true, hypertension may be continuous.

DR. AUB There are several things concerning the adrenal glands that do not satisfy me, but at the same time the things that ought to be considered do not give a high blood pressure. Also, I am puzzled by the rash and the pericardial friction rub. I believe that we must think of either lymphoma or aleukemic leukemia to explain this picture.

DR. MEANS Dr. Aub's point is well taken, and he may turn out to be correct, but it is difficult for me to believe that a lymphoma or a leukemia would produce such a marked elevation of the metabolic rate. My recollection is that Dr. Minot and I once found a fairly close parallel between the white-cell count and the metabolic rate. I do not believe that the ordinary case of lymphoma, with a more or less normal blood picture, has more than a moderate rise in metabolic rate.

DR. AUB That may be true of lymphoma, but aleukemic leukemia may cause a high metabolic rate.

DR. MEANS I suppose that a great deal was going on in the marrow.

DR. MALLORY Dr. Beckman, have you anything to say?

DR. BECKMAN I can only say that this case illustrates the harm of ignorance. I was impressed by the fact that the patient seemed to be so sick. She had lost 40 pounds and had developed heart disease that had gone rapidly into failure during the three months, and I thought that it was probably something akin to lupus erythematosus or rheumatic fever, with severe rheumatic carditis, and was willing to rule out the diagnosis of pheochromocytoma.

DR RAWSON There are three things that I should like to point out. Patients with leukemia and a high metabolic rate studied at the Huntington Hospital usually had large spleens, and the highest basal metabolic rates were observed in patients with so-called "agnogenic myeloid" metaplasia. The white-cell counts were 20,000 or less, with large spleens. I got the impression from some of the patients that a high basal metabolic rate was more related to the size of the spleen than to the white-cell count.

I also want to point out, as Dr Cope has said, that this girl had a friction rub off and on. If the diagnosis of pheochromocytoma is made I think that that, rather than obstruction from tumor, would explain the constipation—the reaction of adrenaline on the smooth muscle of the intestinal tract.

DR. EDWARD F. BLAND I agree with Dr Beckman that this patient was profoundly ill. She presented the picture of severe systemic disease and suggested the possibility of lupus erythematosus without the skin lesions. We also considered severe rheumatoid arthritis and rheumatic fever. The service was more inclined to rheumatic fever, but that possibility did not impress the cardiac group. Dr White's interpretation of the diastolic murmur from its description in the record is perfect. There was a slight diastolic blow along the left sternal border. I saw the patient only once during cardiac rounds and two studies suggested themselves, but I judge that she was too profoundly ill to undertake them. One was a pneumogram, and the other a histamine test. The latter is not without danger.

DR BECKMAN The first one was not done because we could not get rid of the barium.

DR WILLIAM C. BURRAGE I was asked to see this patient because, with Dr Halsted and other members of the Sixth General Hospital, I had seen a case of pheochromocytoma in the military service. The patient was a thirty-two-year-old paratrooper who was being studied for a possible duodenal ulcer. We did a histamine test, employing 0.5 mg of histamine, whereupon he promptly went into apparent collapse. The blood pressure, instead of showing hypotension, was 285 systolic, 160 diastolic. We knew that it had been normal on the previous day. In the course of two or three hours it dropped to normal, but for about two weeks following the episode the patient was quite ill. Electrocardiograms showed minor changes in the T waves and elevation of the ST segment. It is interesting that in 1935, the Mayo Clinic presented an article on the use of histamine intravenously to prove the presence of pheochromocytoma.* Three cases were reported in which the patients were given 0.025 mg of histamine phosphate intravenously, with a systolic rise of at least 120 mm of mercury and with

a concomitant rise in diastolic pressure. It was believed that that was certainly a fair provocative test. We ourselves subsequently repeated the test with 0.02 mg of histamine intradermally and obtained an elevation of 160 mm in the systolic blood pressure. It is fair to say, however, that these patients are subject to sudden death and that the use of this test is not without danger.

DR. CHESTER M. JONES Is it not true that in palpating one of these tumors too vigorously there is a risk as great as the injection of histamine? That risk should be considered before palpation is done.

DR MALLORY I should think so, and the danger also holds for air injection, without which one cannot discover which side the tumor is on.

CLINICAL DIAGNOSES

Intestinal obstruction
Lymphoma?
Rheumatic heart disease?
Pheochromocytoma?
Hypertension

DR WHITE'S DIAGNOSES

Paraganglioma, or pheochromocytoma, with hypertensive heart disease and congestive heart failure
Intestinal obstruction (terminal)

ANATOMICAL DIAGNOSES

Pheochromocytoma left adrenal gland
Cardiac hypertrophy
Pulmonary congestion and edema
Dilatation of cecum and ascending and transverse colon, with fecal impaction
Fibrous pleuritis, old
Emaciation

PATHOLOGICAL DISCUSSION

DR MALLORY Autopsy showed a tumor of the left adrenal gland, between 6 and 7 cm in diameter. On its surface were tiny fragments of cortex. The tumor, arising in the medulla, had grown expansively and had broken the cortex up into scattered fragments, apparently lying in the capsule of the tumor. The heart was markedly hypertrophied, weighing 420 gm, which for a girl of seventeen is extremely large. There was no trace of pericarditis to justify the friction rub. The kidneys were apparently normal grossly and histologically. The tumor histologically was a characteristic pheochromocytoma. There was no mechanical intestinal obstruction. The bowel still contained many large inspissated masses of feces, and the intestinal symptoms were evidently purely those of a maximal grade of constipation.

*Roth, G. M., and Kvale, W. F. Tentative test for pheochromocytoma (using histamine injections). *Am J M Sc* 210: 653-660, 1945.

CASE 32512

PRESENTATION OF CASE

A fifty-nine-year-old insurance executive entered the hospital because of an attack of "indigestion" followed by dyspnea and vomiting.

Six months previously the patient had had an attack of chest pain radiating down the left arm. A physician took an electrocardiogram, but details of the results were not available. The patient was placed on strict bed rest for six weeks, after which he was gradually permitted to get up and move around for the next week and a half. At about that time he had an episode of mental depression and a fear of going anywhere. No objective neurologic signs were noted. Three and a half months later, he started going to his office for two hours daily and gradually increased the time until just before the admission, when he was spending five and a half hours a day at the office.

Nineteen hours before admission the patient was awakened by an attack of "indigestion" but the pain soon moved up into the chest and radiated down the left arm, three hours later he became short of breath and vomited. Two and a half hours later he began to spit up frothy red material and his breathing sounded as if the throat were "full of water." A physician found the blood pressure to be 70 systolic, 40 diastolic, and the pulse to be 130, 15 mg of morphine was given. Nine hours later, 12 mg of Purodigin was administered. About an hour before admission the blood pressure had risen to 100 systolic, 70 diastolic, but the pulse remained at 130 and the patient was orthopneic. There were a few rales in the lungs, the heart sounds were distant, and there was a regular, gallop rhythm. At about that time bloody urine was passed.

On admission the heart was slightly enlarged to the left, and the sounds were faint and distant, with a regular gallop rhythm of 140. Persistent moist rales were heard throughout both lung bases, extending half way up the scapulas. The liver was barely palpable and questionably tender. There was no edema of the lower extremities.

The blood pressure was 100 systolic, 80 diastolic. Examination of the blood showed a hemoglobin of 16.0 gm and white-cell count of 23,000, with 92 per cent neutrophils. The urine had a specific gravity of 1.020 and gave a + test for albumin. The sediment contained frequent hyaline casts, rare red cells and 3 white cells per high-power field. X-ray examination revealed extensive, mottled, hazy density throughout both lungs, most pronounced in the middle and lower lung fields. The left leaf of the diaphragm and the outline of the left side of the heart were obscured.

An electrocardiogram (cardiette) taken on admission revealed a sinus tachycardia of 180. Low QRS voltage was greatest in Lead 3, where it measured 2.5 mm. There was an S wave in Lead 1 equal to

1 mm, and right-axis deviation was present. T_1 and T_{CF_1} were slightly inverted, T_2 - and T_{CF_2} were flat, T_3 was diphasic and T_{CF_3} was upright. There were small R waves in Leads CF_2 and CF_4 and no R wave in Lead CF_1 . A Q wave equal to 3 mm was noted in Lead CF_1 . A second tracing taken the next day revealed a somewhat increased rate, the T wave in lead CF_1 had become much lower.

On the second hospital day a venesection was performed, and 500 cc of blood was withdrawn. This resulted in improved breathing, but during the same evening breathing again became difficult and moist bubbling rales were heard throughout both lung fields. The pulse became weak, and the apical pulse was 150. The downhill course continued, two days later the blood pressure was 94 systolic, 80 diastolic. The pulse was 140 and weak but regular. Respirations were 40, and there was slight cyanosis despite oxygen administration. The patient died quietly on the fourth hospital day.

DIFFERENTIAL DIAGNOSIS

DR HOWARD B SPRAGUE This record appears to be fairly straightforward, but the history is often deceptive. The first episode seems to be quite clear cut. Out of a clear sky, six months before the fatal illness, this man had had an attack of pain in the chest radiating down the left arm, it was sufficiently characteristic to suggest that he should have an electrocardiogram, whose results we do not know, but he received the textbook treatment for coronary thrombosis with myocardial infarction — bed rest for six weeks. The mental depression and fear of going anywhere are frequent in patients recovering from myocardial infarction. This patient, however, was able to go back to his work. We do not know whether, during the next period before the fatal attack, he had residual difficulties, such as angina on effort and dyspnea. He was then awakened by an attack of indigestion. It is noticeable that on each occasion there was the same pattern of indigestion, dyspnea, vomiting and radiation of pain down the arm. Shortly thereafter the patient developed pulmonary edema, with frothy sputum and a marked fall in blood pressure. Throughout this final fatal episode he had an extremely rapid tachycardia and a gallop rhythm was prominent. There was evidence of left ventricular failure and a marked increase in the rate, so that one can assume that two mechanisms produced the gallop rhythm, which was probably a "summation gallop rhythm," as it is called — namely, a third sound mechanism during the early stage of left ventricular filling superimposed on whatever sound is produced by auricular contraction.

At that time bloody urine was passed. I do not know whether that is significant, but it was later revealed that there were red cells in the sediment. The patient entered the hospital in shock, with faint and distant heart sounds, a low blood pressure, a

gallop rhythm and tachycardia. May we see the x-ray films?

DR JAMES R. LINGLEY: There is extensive density on both sides of the chest, as described in the record. The density is hazy and involves the greater portion of both lungs. I think that the appearance is consistent with edema. I interpreted these films and was disturbed by this shadow at the left base, which I thought could possibly be due to an infarct, but so much edema is present that I do not believe that one can be certain.

DR SPRAGUE: Can you say anything about the heart size? The record states that the heart was slightly enlarged clinically.

DR LINGLEY: I think that it probably was.

DR SPRAGUE: The high white-cell count and the urinary findings seem to be consistent with a combination of shock and cardiac failure, although we must think of renal infarcts in such a situation. The electrocardiogram, which we must take as described in the record, is confusing. When we have, as we assume to be true in this case, more than one myocardial infarction, the electrocardiogram often loses its characteristic pattern, and the findings produced by the previous infarction are probably masked by the second one. A definite finding is the low-voltage electrocardiogram, with inversion of the T waves in Leads I and CF₆, which is out in the axilla, and rather small R waves in the leads taken to the left of the sternum and at the apex, there was no R wave in Lead CF₆. These findings are consistent with myocardial infarction of the anterior and apical type, probably rather lateral in position. I shall discuss that later. If we can assume that the T waves in Lead CF₆ became lower, at least extension of the electrocardiographic abnormalities toward the midline is indicated.

A venesection was performed. The patient's breathing was improved, but he died on the fourth hospital day.

There are a few things that bother me. In the first place, the pulse rate went up to 180, and the next day it was somewhat faster. That is an extreme degree of sinus tachycardia — in other words, a normal mechanism. It suggests that this was ectopic auricular tachycardia, perhaps an auricular flutter. Although normal sinus tachycardia can occur at this rate and since in this case the pulse varied apparently in steps between 130 and 180, this was probably a sinus mechanism rather than an abrupt change from a rapid ectopic tachycardia to a sinus tachycardia that was considerably slower. The electrocardiogram seems to me to reflect an infarction involving the anterior and apical regions of the heart, later complicated by posterolateral involvement. The T-wave depressions in Lead I and in the chest leads characteristic of anterior and apical infarction may be partly masked by changes in the posterior wall of the heart. A patient may die of myocardial infarction with a more normal

looking electrocardiogram just before death than during the time of the first infarction. Because the auricle in this case showed such an extreme irritability, was there also auricular infarction? Auricular infarction is an extremely difficult condition to diagnose. It seems to be associated with abnormalities in auricular rhythm, such as auricular fibrillation, auricular flutter and changes in the T waves of the auricle. The T waves of the auricle are not ordinarily seen unless auriculoventricular block is present to separate the auricular complexes from the ventricular, and to allow one to see the normal inverted T waves. In a few cases of auricular infarction described in the literature these auricular T waves have become upright.

The question of pulmonary infarct always arises in cases of this sort. Statistically we are justified in saying that pulmonary infarction occurs. I bring the possibility of pulmonary infarction into the discussion only to reject it. At least, this sudden episode suggests pulmonary edema and left ventricular failure. There had been no pain in the chest, and the character of the sputum was consistent with acute pulmonary edema. It is possible that there was a renal embolism, which brings up the question whether or not following the original infarction a mural thrombus of the ventricle was a source for emboli. One would certainly be brave to suggest that six months after an infarction this man had a coronary embolus from the left ventricle. The first case, I believe, in which the diagnosis was suggested clinically was described by Dr Louis Hamman* shortly before the war, the patient, a young woman without heart disease who was thought to have coronary embolism from thrombi in the pulmonary veins during a respiratory infection, recovered, and the diagnosis was not proved. It is much more probable that in the case under discussion there was an extension of a severe degree of atherosclerosis and occlusion of the coronary tree. I therefore believe that the patient had a myocardial infarction involving the left ventricle, probably the anterior apical portion first, that he later had an extension — probably laterally — that resulted in a wide degree of infarction of the left ventricle, that the findings do not suggest septal involvement unless it was in the anterior part of the septum and that there were probably mural thrombi of the left ventricle, there is a vague possibility of involvement of the auricle by infarction and of infarcts in the kidney.

DR ROBERT S. PALMER: Does the right-axis deviation in the electrocardiogram make you think more seriously of pulmonary embolism than of infarction?

DR SPRAGUE: Of course that entered my mind, but a high percentage of patients developing anterior infarction have a shift of the electrical axis to the right. It is true that those who have a posterior

*Hamman L. Coronary embolism. *Am Heart J* 21:401-422 1941

infarction have a higher percentage of shift of the axis to the right, but I have decided against infarction of the posterior part of the septum. The right-axis deviation was possibly due to one of at least three mechanisms. I was willing to discard pulmonary embolism as the cause.

DR. BENJAMIN CASTLEMAN: Is not right-axis deviation in cases of myocardial infarction most frequently due to septal involvement, with bulging into the right ventricle?

DR. SPRAGUE: Such a situation is likelier with posterior involvement of the septum. There has been some argument about the mechanisms of this shift of axis. I should hesitate to make a diagnosis of posterior septal infarction, because we have no indication of bundle-branch defect or auriculo-ventricular block, which would be fairly likely.

DR. LOWREY F. DAVENPORT: In a case that came up for discussion on the surgical service the question was raised whether one is likelier to find coronary infarction with a normal electrocardiogram or pulmonary infarction with a negative x-ray examination. What is your experience?

DR. SPRAGUE: I think that pulmonary infarction with a negative x-ray examination is more probable.

DR. TRACY B. MALLORY: Do you want to challenge that remark, Dr. Lingley?

DR. LINGLEY: No.

CLINICAL DIAGNOSES

Coronary heart disease

Acute myocardial infarction

DR. SPRAGUE'S DIAGNOSES

Old coronary occlusion, with infarction of anterior apical region of left ventricle

Fresh coronary occlusion, with infarction of posterolateral area of left ventricle and mural thrombi of left ventricle

Possible infarction of anterior part of inter-ventricular septum, with auricular infarction and renal infarcts

ANATOMICAL DIAGNOSES

Coronary sclerosis, with recent thrombosis of circumflex branch of left coronary and old recanalized thrombosis of descending branch of left coronary artery

Myocardial infarction, recent, massive posterolateral aspect of left ventricle

Myocardial infarction, healed, apical, with mural thrombus

Arteriosclerosis, generalized, moderate

Pulmonary edema, acute, massive

PATHOLOGICAL DISCUSSION

DR. MALLORY: Autopsy showed a hypertrophied heart, which weighed 500 gm., and as Dr. Sprague

predicted, evidence of two episodes of infarction of the myocardium. The anterior surface of the left ventricle and the adjacent part of the inter-ventricular septum showed an old dense fibrous scar consistent with an infarction six months previously. Overlying this area was a large mural thrombus, which was partially organized. The fresh infarction was in the posterolateral aspect of the left ventricle, and the two infarcts together involved approximately two thirds of the entire ventricle. Little living musculature remained. There were two points of occlusion in the coronary arteries, which could be correlated with the separate myocardial lesions. In the descending branch of the left coronary artery was an old area of narrowing with calcification that seemed to have a trace of recanalization no wider than 0.5 mm. in diameter, in the circumflex branch a fresh thrombus, about 1 cm. in length, was still red and had evidently caused the second episode.

The lungs were rather interesting. They were markedly and diffusely edematous, the combined weight being 1900 gm. They did not present the usual appearance of acute pulmonary edema of cardiac origin. The transudate into the alveolar sac is ordinarily a thin watery fluid, such as the frothy fluid coughed up by this patient at the initial episode. At the time of death, however, the alveoli were filled with a protein-rich fluid, which in fixation coagulated almost like thyroid colloid and in which large numbers of red cells were found. There were a number of tiny thrombi in the small arterioles, but no gross pulmonary emboli. Nothing was found that could be called an infarct of the lung, but I believe that the patient did have a shower of minute pulmonary emboli. Since no gross infarcts were found we did not explore the leg veins in this case. I cannot say what the source was, but I think that sometime during the last day or two of life, a shower of minute emboli probably changed the character of the pulmonary findings, although it did not produce frank infarction. Because of the hematuria we were interested in the kidneys but found nothing whatever.

DR. SPRAGUE: These pulmonary findings could not be explained on a thrombotic basis?

DR. MALLORY: Perhaps they could be. I am unable to decide, but at any rate it is an unusual phenomenon.

DR. SPRAGUE: You have not seen that with ordinary congestive failure?

DR. MALLORY: These lungs looked more like those seen in acute nephritis than the lungs of cardiac failure.

DR. SPRAGUE: The posterior septum was not involved?

DR. MALLORY: No.

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CHRISTMAS 1946

THERE can be no beginning without an ending, no ending without the commencement of something new. A successful termination of the process of gaining an education in a properly constituted hall of learning was once termed, by some inspired educator, a commencement. It is, for the individual, the ending of a probationary period and the beginning of a new phase of personal existence, the conclusion of a somewhat rudimentary activity and the inauguration of a broader experience. Life is full of commencements and graduations and closing of books and opening of new accounts and endings and beginnings.

And so Christmas, which marks the beginning of a new era, annually reaffirmed, marks also the end-

ing of an older period that has made its contributions to the progress of man and is ready to depart.

Christmas, not so many years ago, was considered a pagan festival by our unctuously righteous forefathers, and indeed it was, in its fundamentals, just that. Marking approximately the end of the season of shortening days and the almost imperceptible beginning of the sun's return, it was an important date on the calendar in the forests of northern Europe, where the days were short and cold and the nights were long and dark.

Its Christian significance goes back to the second century A.D., when the birth of Christ began to be celebrated, and it is reported that the Emperor Diocletian, learning that a number of Christians were commemorating this blessed event, set fire to the building, whereby they all perished.

The Christian cycle developed in the fifth to eighth centuries, in which the winter solstice, celebrated by all nations as marking the renewal of life in nature, was appropriately accepted by the Church as the time to celebrate also the dawning of a new spiritual light on the earth. Since that period we have had dual forms of observance: the deeply religious ritual of the Christian Church, combined with the merrier pagan reaction to a faint promise of spring—a convenient association, but frowned on by our ancestors, the Puritans.

The customs of Christmas, of which the Merry Christmas that we now wish our readers is not the least important to us, are too firmly fixed for their origins to detract from the supreme value of the day. It is the day of that good will which may yet allow us to live together in harmony. It is the day on which we settle the accounts of a dying year and look forward, perennially optimistic, to a new year, of which more anon.

FALSE PROPHET

ON November 11, 1943, the *Journal* acknowledged the passing of another milestone in the long struggle to ensure a safe and satisfactory milk supply for the population of the Commonwealth. This particular milestone was a newly adopted regulation of the Boston Health Department, effective on September 30 of that year, putting an end to the sale of raw milk in the City of Boston, regardless of its source.

Some years earlier the sale of all raw milk in the city, unless certified by the Boston Medical Milk Commission, had been prohibited, in 1930 the commission, on its own initiative and against the opposition of the American Association of Medical Milk Commissions, had voted to permit the pasteurization of milk on farms under its certification. The association now accepts the pasteurization of certified milk, and the Boston commission requires it

And so the slow steps have been taken leading toward as safe a milk as can be procured for as large a percentage of the population as possible, with the knowledge always before us that bacterial contamination makes milk unsafe—contamination not only with the tubercle bacillus and *Brucella abortus* but also with the streptococcus, the typhoid bacillus, the dysentery-producing organisms and many others

It leaves us aghast, therefore, to read in the November 5 issue of the *Boston Traveler* in "Personal Health Service," a column contributed by William Brady, M.D., not only the author's unique classification of milk but also his reasons for defending that classification against all comers

Dr Brady's classification of the grades of milk is as follows: first choice—certified milk, second choice—Grade A raw milk from a tuberculin-tested herd, and third choice—any fresh milk, scalded or boiled one minute. "Any old milk," according to Dr Brady, "regardless of its source, quality or purity, is made safe for infant, child, invalid or adult by scalding, that is, by bringing to a boil and boiling for one minute." (The accepted definition of scalding is bringing to a boil, the one minute is Dr Brady's contribution.)

Dr Brady's two reasons for placing raw milk in first and second places (he apparently assumes that certified milk is necessarily raw) are that undulant fever from ingested milk is a rare disease, and that

raw milk in his opinion tastes better than parboiled or scalded milk. Although at one point he mentions pasteurized milk, indicating that he is aware of its existence, it nowhere enters into his classification. It is not by chance that all the milk now legally sold in Boston and a large percentage of that distributed elsewhere in the Commonwealth are pasteurized.

The pasteurization of milk, even of clean milk, needs no justification in these columns, nor is it possible

anywhere to justify the use of dirty milk, even when sterilized, if clean milk can be made available. Supposedly pure milk may become contaminated with pathogenic organisms, and pasteurization makes assurance of purity doubly sure. This fact has been accepted by public-health authorities for years.

Dr Brady is certainly welcome to his own opinions on these matters so long as he keeps them

to himself. When he uses the pages of newspapers to advocate dangerous and discarded principles, however, some effort should be made to protect the public from his irresponsible doctrines.

MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

MASSACHUSETTS MEDICAL SOCIETY DEATHS

BARKER—Williston W. Barker, M.D., of Dorchester, died November 26. He was in his sixty-fifth year.

Dr Barker received his degree from Harvard Medical School in 1906. He was a member of the New England Pediatric Society and a fellow of the American Medical Association.

His widow, two sons and a daughter survive.

HUTCHINSON—Charles M. Hutchinson, M.D., of Cambridge, died November 26. He was in his seventy-seventh year.

Dr Hutchinson received his degree from Dartmouth Medical School in 1894. He was a fellow of the American Medical Association.

His widow and a daughter survive.

MORGAN—Charles R. Morgan, M.D., of Medford, died November 28. He was in his sixty-ninth year.

Dr Morgan received his degree from Tufts College Medical School in 1907. He was a fellow of the American Medical Association.

His widow, two sons and three daughters survive.

MOULTON — Allen T Moulton, M D, of Boston, died November 22 He was in his fifty-seventh year

Dr Moulton received his degree from University of Maryland School of Medicine and College of Physicians and Surgeons in 1911

His widow survives

PHELPS — John S Phelps, M D, of Lynn, died December 3 He was in his eighty-first year

Dr Phelps received his degree from Harvard Medical School in 1893

A niece and two nephews survive

ROY — Joseph N Roy, M D, of Webster, died March 19 He was in his seventy-fifth year

Dr Roy received his degree from Baltimore University School of Medicine in 1902 He was a fellow of the American Medical Association

A HUNDRED YEARS AGO

A circular has been issued by a committee of the Berkshire Medical District, addressed to the profession of Massachusetts, in which are set forth, in plain language, the grievances of the practitioners on the west side of the mountain They apprise all whom it may concern that an application will be made to the Legislature, the next session, praying that the Massachusetts Medical Society may be reorganized, and in default of such re-organization, that the profession in the County of Berkshire may be constituted a separate and distinct medical society The fact is, the opinion is entertained that all the essential executive officers are invariably held by persons in Boston, or near by — and as some of the malcontents have often asserted, their portion of the members are only parts and parcels of the medical machinery to hold up one or two men before the community as those whom the multitude of doctors delight to honor They say, too, that the old trick of serving out sop by giving the interior of the State a *vice*-president, occasionally — a post that no one covets — will no longer work All this has frequently been sounded in the ears of the Fellows on anniversary meetings, but it produced no amelioration, and now a desperation is manifested that will certainly re-make or break the old Society — As the Boston dentist Dr J F Flagg says, everyone who has any sympathy for human suffering and all who are called upon professionally to perform painful operations must feel desirous to avail themselves of the means of diminishing or destroying that state of consciousness which recognizes all violence done to the sensitive tissues of the body, while such operations are in process He understands, however, that the free use of the *letheon* has been ceded only to the surgeons of the Massachusetts General Hospital In spite of Dr J C Warren's admonition that the *letheon* should never be employed except under the inspection of a judicious and competent person, he asks why, if he or any other reputable practitioner wishes to avail themselves of any of the

possible effects of an article of the materia medica, they must purchase the right to use it and use it as a patent medicine? — A Fellow writing anonymously asks whether any patent has been obtained for the *modus operandi* of reconciling the principles and avowed objects of the Massachusetts Medical Society with the recent practice of some of its leading members He suggests that as new patents come out for new discoveries in medicine, the country practitioners might take turns with the city practitioners in writing the puffs and paying for the patent, exercising, of course, all due meekness and quietness while the patenting business is going on — Dr J D Mansfield of South Reading says that it seems to him not only ridiculous but absolutely wrong for any physician to adopt a course of action so entirely contrary to the spirit of the rules of the Massachusetts Medical Society as that assumed by the Boston surgeons Physicians in his vicinity, he is satisfied, will use the ether if they have occasion so to do, and if ether alone does not answer the purpose they can easily find a compound that will do as well as the *patented* vapor — Dr A L Pearson of Salem disagrees with such views Having used the new gas successfully in three cases, he believes that Dr Morton and Dr Jackson, at least, are entitled to the hearty thanks of the profession for their discovery If some hunter up of obsolete theories should prove that such a thing had before been thought of, or tried, still these gentlemen are entitled to the credit of having made it, for the first time, perfectly available to the suffering, and submitted it to the test of those competent to decide on its merits, without being content to rest its pretensions on nonprofessional credulity or popular notoriety — Dr Henry J Bigelow reports that a few days since, he tied the Femoral Artery of a patient who was unable to pay for the operation He found no difficulty in obtaining the gratuitous use of the ethereal vapor, nor could he conceive that others would in similar circumstances — We learn that in the United States with a population of 20,000,000 of people, there are about thirty medical schools, in which there are probably an average annual number of 4500 students, 1300 of whom are yearly graduated No wonder there is such a prodigious competition for professional existence — It seems that the War Department may be somewhat annoyed by persons wishing employment as surgeons in the Army What will become of all the young doctors if some outlet is not found for them? — Dr Nathan Holmes, of St Louis, Mo, announces that whiskey, or any other stimulus, freely given till there is a high pulse, will cure the bite of the rattlesnake He says that he doubts whether fifty rattlesnakes could poison a man when fully drunk — Smallpox is again creeping on toward New England Dr Thomas Sanborn of Newport, New Hampshire, reports ten cases in Goshen, all vaccinated several years pre-

virus, but probably with impure virus. In a great number of exposures to varicellous contagion, not a single one of those vaccinated on the day or previous to exposure had the varcoloid and no bad consequences resulted. — Another great discovery is announced in France by M. Pelouze, the chemist, viz, priming gun cotton with fulminating mercury. The same great man proposes to feed mankind on wood. Old bedsteads, broken chairs, and fractured table legs yield, it is said, azote enough to sustain the invading army of Mexico. — As usual there is an excellent class in attendance on the medical lectures at Yale College, the present season. The number does not equal some other institutions, but in no place is the course of instruction more perfect or thorough. — Extracted from the *Boston Medical and Surgical Journal*, December, 1846

R F

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

FREE WHOLE BLOOD THROUGH HOSPITALS

Several Bay State hospitals are now co-operating with the Massachusetts Blood Donor Program by providing free, whole blood to all patients, regardless of their financial status. (Hospitals may continue to charge their usual fee for administration.) Under this plan, the hospital blood banks operate in much the same manner as previously, except for the following changes:

Relatives of patients are asked to replace only one pint of blood for each unit required for the patient. Current donations to the hospital blood bank are considered as contributions to the state program.

The Department of Public Health sends regular supplies of whole blood to maintain these banks at a safe level; these supplies represent a return to the community of the blood donated by residents of the community through the Mobile Unit.

The list of hospitals that have adopted this program is as follows:

Burbank Hospital, Fitchburg
St. Luke's Hospital, New Bedford
Hillcrest Hospital, Pittsfield
House of Mercy Hospital, Pittsfield
St. Luke's Hospital, Pittsfield
Waltham Hospital, Waltham
Westfield State Sanatorium, Westfield
Addison Gilbert Hospital, Gloucester (to begin as soon as installation of refrigeration equipment is completed)

Any hospital desiring to set up a free, whole-blood program should work out preliminary arrangements with the local chapter of the American Red Cross. After initial plans are drawn up, the State blood laboratory should be consulted regarding final arrangements whereby the whole blood can be supplied to the hospital.

MOBILE-UNIT VISITS

The Mobile Unit of the Massachusetts Blood Donor Program will make the following visits during late December and early January:

PLACE	DATE
Wilmington	December 30 and 31
Haverhill	January 7, 8 and 9
Weymouth	January 14
Lowell	January 15, 16 and 17

BOOK REVIEWS

Acute Injuries of the Head: Their diagnosis, treatment, complications and sequelae. By G. F. Rowbotham, B.Sc. (Manchester), F.R.C.S. (Eng.). With a foreword by Norman M. Dott, M.B., Ch.B. (Edin.), F.R.C.S. (Edin.). 8°, cloth, 424 pp., with 201 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$8.50.

This book was first published in 1942 in England, where it has since enjoyed a well deserved popularity. There, as in the United States, neurosurgeons are few and far between outside the large medical centers, and the majority of head injuries are treated by general surgeons, for whom this volume is an excellent guide. Profusely and beautifully illustrated, it leaves no question of pathology, diagnosis, treatment or operative technique unanswered. Although American neurosurgeons may disagree with certain aspects of the answers, the basic principles are beyond argument. The crisp, clear text is characteristic of the best British medical writing. The book is highly recommended to students and interns as well as to all who treat head injuries.

The Art of Medicine in Relation to the Progress of Thought: A lecture in the history of science course in the University of Cambridge, February 10, 1945. By A. E. Clark-Kennedy, M.D., F.R.C.P. 12°, paper, 48 pp. Cambridge, England: University Press, 1945. 75 cents.

Clark-Kennedy, in this lecture delivered at Cambridge University, briefly reviews the evolution of medicine from Hippocrates to the present time. The Hippocratic period, from the sixth century B.C. to the death of Galen at the end of the second century B.C., was notable for three great contributions: the observation of disease as an objective phenomenon and the keeping of accurate records of cases, the development of high moral standards and the adoption of an ethical code, the Hippocratic oath, and the establishment of the idea of the physician as a necessary aid to living in human society. The Renaissance period, beginning with the publication of the anatomy of Vesalius in 1543 and ending with the publication of the first complete book on physiology of the human body by René Descartes, was notable for the work of Leonardo da Vinci, Vesalius, William Harvey, Malpighi, Descartes and Sydenham and for the advance of surgery. The third period, which comprises roughly the last hundred years and is notable for many great contributions to biology and medicine, includes Darwin's *Origin of Species*, Pasteur's disproof of the spontaneous generation of life, the discovery of the bacterial cause of many diseases, Virchow's theory of cellular pathology, Mendel's work on genetics, Lister's antiseptic and aseptic surgery, Pavlov's description of conditioned reflexes, Freud's chemotherapy, increasing knowledge of viruses and genes and the discoveries of insulin, the sulfonamides and penicillin.

Clinical Neurology. By Bernard J. Alpers, M.D., Sc.D. (med.). 4°, cloth, 797 pp., with 232 illustrations and 58 tables. Philadelphia: F. A. Davis Company, 1945. \$8.00.

The subject of neurology is fully covered in this new textbook by a qualified author that is aimed to give medical students and practitioners a full knowledge of the neurologic conditions likely to be encountered in practice. The text is clear, the material is well organized, the illustrations in general are excellent, and there is a good index. Many will miss references to the literature, but for the audience that the author had in mind, the book is a satisfactory one and

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PROBLEMS ARISING IN THE TREATMENT OF SYPHILIS WITH PENICILLIN

WILLIAM R. HILL, M.D.*

BOSTON

THIS report deals with the therapeutic pitfalls encountered in 125 patients with various types of syphilis who were treated with penicillin at the Massachusetts General Hospital subsequent to November, 1944. All these patients were hospitalized and treated for periods ranging from eight to fifteen days. Penicillin in aqueous solution was administered intramuscularly in doses of 20,000 to 40,000 Oxford units every three hours, day and night. The total dose was from a minimum of 1,200,000 to 2,400,000 Oxford units. Arsenicals and bismuth were not used concomitantly with penicillin, but in most patients with interstitial keratitis or neurosyphilis, fever therapy supplemented the treatment with penicillin.

PENICILLIN RESISTANCE

Late Syphilis

In this series the majority of patients with late syphilis who had exhibited persistently positive serologic reactions (Wassermann fastness) and who had received adequate treatment with arsenicals and bismuth before penicillin therapy was begun failed to show an appreciable reduction in the serologic titer. Occasionally, a negative serologic reaction was noted immediately following penicillin therapy. Re-examination some months later showed that the change was only temporary.

The results in the cases of acute interstitial keratitis treated with penicillin were unpredictable. Penicillin alone was administered to 3 patients in total doses of 1,200,000 to 2,400,000 Oxford units. This was combined with malaria therapy in 1 case and with typhoid vaccine to produce fever in another. Two patients who were treated with penicillin alone experienced favorable clinical results, no subjective or objective improvement was noted in the remaining 3. One patient, who improved clinically and in whom, after ten months' follow-up study, a serologic reversal was obtained, had been treated with a total dose of 1,200,000 Oxford units of penicillin alone.

Three patients who had advanced optic atrophy — 1 with congenital, and the other 2 with acquired syphilis — failed to respond clinically to a total dose of 2,400,000 Oxford units, which each received over a period of eight days. No improvement in the visual fields had been noted six months after therapy had ended. One patient with deafness due to involvement of the eighth cranial nerve was treated with 1,200,000 Oxford units but did not respond favorably.

None of the 5 patients with neurosyphilis with lightning pains showed any change in the character or intensity of the pains following treatment with a total dose of 2,400,000 Oxford units of penicillin. One patient who had neurosyphilis and gastric crises did not benefit when a total dose of 900,000 Oxford units was given intrathecally, together with 2,400,000 Oxford units by the intramuscular route.

O'Leary, Brunsting and Ockuly¹ reported no improvement in gastric crises, ataxia or incontinence in persons with neurosyphilis, nor was clinical improvement noted in their cases of early dementia paralytica in which penicillin alone was given.

Favorable results have been reported in late cutaneous syphilis.² Recently, however, I have had the opportunity of examining a patient with an extensive destructive gumma involving the center of the face, including the nasal septum, and hard palate who had received 2,400,000 Oxford units of penicillin before admission, without improvement. Therapy with induced malaria completely resolved the lesion.

Early Syphilis

We have noted no evidence of penicillin resistance in this type of case. Tyson,³ however, reported the case of a colored man who had primary syphilis. The dark-field examination was positive. He was treated with a total dose of 2,400,000 Oxford units of penicillin intramuscularly in the course of four days. The penile lesion did not heal. *Treponema pallidum* was seen on dark-field examination of the lesion four months later. At that time, also, lesions of secondary syphilis were present and a

*Assistant in medicine and in dermatology, Harvard Medical School; assistant physician and assistant in dermatology in charge of the South Medical Clinic (Syphilis), Massachusetts General Hospital.

unusually free from errors. It is not an unusual book but rather a standard text, similar to many that have been published in the past. The author has shown excellent discrimination in selecting the illustrations and in making the text readable. The book, however, is not distinguished in the sense that it presents a new point of view, its value lies in the careful methods used to analyze the principles of neurologic syndromes, particularly as they appear in the more frequent pathologic conditions.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Pathology of Tropical Diseases. An atlas. By J. E. Ash, M.D., director, Army Institute of Pathology, Army Medical Museum, and Sophie Spitz, M.D., pathologist, Army Institute of Pathology, Army Medical Museum. 4°, cloth, 350 pp., with 941 illustrations. Philadelphia: W. B. Saunders Company, 1945. \$8.00.

This new atlas has been written to fill a gap in the literature of tropical diseases. An introductory text precedes each series of illustrations. Emphasis has been placed on diseases that have proved to be of greatest significance from a military standpoint and that are likely to be of importance to the civilian profession. Illustrations are based on the collections of the Army Institute of Pathology in the Army Medical Museum, with additional material from civilian sources. This work should prove valuable as a reference source in its particular field.

A Manual of Surgical Anatomy. Prepared under the auspices of the Committee on Surgery, Division of Medical Sciences, National Research Council. By Tom Jones and W. C. Shepard. 12°, cloth, 254 pp., illustrated. Philadelphia and London: W. B. Saunders Company, 1945. \$5.00.

This manual of surgical anatomy completes the series of military surgical manuals edited by the Committee on Surgery of the National Research Council and primarily intended for the use of medical officers of the United States Army and Navy. The volume consists of one hundred and thirty-nine pages of illustrations and one hundred and fifteen pages of an explanatory index. This small manual should prove valuable to medical students and civilian surgeons for ready reference purposes.

Doctors at War. Edited by Morris Fishbein, M.D., chairman of the Committee on Information, Division of Medical Sciences, National Research Council. 8°, cloth, 418 pp., with 82 illustrations. New York: E. P. Dutton and Company, Incorporated, 1945. \$5.00.

This collective work makes available the personal accounts of many of the medical leaders who directed the work of vital military and civilian agencies during the war years. The whole field of military medicine is covered from Selective Service to rehabilitation centers. Chapters are also included on the medical activities of the Veterans Administration, the American Red Cross and the National Research Council during World War II. This book, written by sixteen leading authorities responsible for organizing medical welfare, is intended for the layman as well as the doctor and should be in all public and medical libraries and should prove interesting to all physicians. The text is excellently edited by Dr. Fishbein and is well printed with a good type on good paper.

A Textbook of Neuro-Anatomy. By Albert Kuntz, Ph.D., M.D., professor of microanatomy, St. Louis University School of Medicine. Fourth edition, thoroughly revised. 8°, cloth, 478 pp., with 325 illustrations. Philadelphia: Lea and Febiger, 1945. \$6.50.

This third edition of a standard reference work has been thoroughly revised and enlarged in the light of new knowledge gained through the efforts of many investigators working during the period since the publication of the second edition. The

text has been in part reorganized and rewritten, and an attempt has been made to incorporate the essential findings recorded in the recent literature. This text should be in the libraries of all neurologists and medical reference collections.

Howell's Textbook of Physiology. Edited by John F. Fulton, M.D., Sterling Professor of Physiology, Yale University School of Medicine. Fifteenth edition. 8°, cloth, 1304 pp., with 507 illustrations. London: W. B. Saunders Company, 1946. \$8.00.

This fifteenth edition of Howell's textbook should be considered a new textbook of physiology, since it is the joint work of twenty-four contributors, edited by Dr. Fulton, the first fourteen editions were written solely by Dr. Howell. The various contributors, all authorities in their particular field, have brought their subjects up to date, including the knowledge gained during World War II. Many new chapters have been added, and many others have been rewritten in their entirety. This new text should prove of value as a standard reference work.

The Autonomic Nervous System. By Albert Kuntz, Ph.D., M.D., professor of microanatomy, St. Louis University School of Medicine. Third edition, enlarged and thoroughly revised. 8°, cloth, 687 pp., with 91 illustrations. Philadelphia: Lea and Febiger, 1945. \$8.50.

This fourth edition of an authoritative text has been thoroughly revised and in part rewritten. The text has not been materially extended, although new material has been incorporated, including more complete and accurate accounts of the anatomic and functional relations of the diencephalon and the corpus striatum and the conduction pathways for visceral impulses. Also, new data concerning cortical projection areas, the connections of subcortical centers with the cerebral cortex and the relation of these centers in the extrapyramidal projection system, the arrangement of the cortical neuron, the synaptic connections of afferent fibers within the cortex and the functional relation of cortical neurons with one another are included. The book is well printed on good paper with a good type and should be in the reference collections of all neurologists and medical libraries.

A Textbook of Surgery. By American authors. Edited by Frederick Christopher, M.D., associate professor of surgery, Northwestern University Medical School, and chief surgeon, Evanston (Illinois) Hospital. Fourth edition, revised and reset. 4°, cloth, 1548 pp., with 1483 illustrations on 762 figures. Philadelphia and London: W. B. Saunders Company, 1945. \$10.00.

This fourth edition of a standard authoritative composite text on surgery, first published in 1936, has been thoroughly revised and reset. Two important new sections have been added, one on military surgery and the other on chemotherapy and surgical infection, including the use of penicillin and the sulfonamides. Other entirely new sections include actinomycosis, burns, shock, indolent ulcers, vascular-tissue tumors, tumors of the sympathetic nervous system, fractures of the radius and ulna, tumors of the breast, inflammations of the chest wall, wounds of the thorax, pilonidal sinuses and cysts, the peritoneum, diverticulitis and ulcerative colitis, unusual hernias, diverticula of the urinary bladder, diseases of the vulva and vaginal fistula. This work should prove valuable as a reference source to all physicians and surgeons and should be in all medical libraries.

Principles of Dynamic Psychiatry, including an Integrative Approach to Abnormal and Clinical Psychology. By Jules H. Masserman, M.D., Division of Psychiatry, Department of Medicine, University of Chicago. 8°, cloth, 322 pp., with 4 plates. Philadelphia and London: W. B. Saunders Company, 1946. \$4.00.

The purposes of this work are to provide an orientative introduction to the principles of modern dynamic psychiatry, to outline the applications to the techniques of clinical diagnosis and to demonstrate the rationale and methods of effective therapy.

(Notices on page xvi)

of the disease by penicillin but became reinfected after his wife developed the lesion

In both relapse in early syphilis and reinfection, retreatment should consist of double the previous dose or more, with the addition of arsenic and bismuth. For data on this phase, reference to a report of the Committee on Medical Research and the United States Public Health Service¹² is advised. The decision to retreat usually arises between the third and the twelfth month following the original therapy.

REACTIONS

Although the incidence of severe reactions is insignificant when compared with those attending routine treatment with arsenic and bismuth, reactions do occur among patients treated with penicillin.

Shocklike Reactions

The Herxheimer reaction was noted in 75 per cent of patients with early syphilis in this series. In such cases, within the first eight hours and most frequently after the second injection, a rise in temperature to from 100 to 103°F occurs. The patient complains of chilliness, headache, backache and malaise. There may be an exacerbation of pre-existing lesions. This does not call for discontinuation of therapy. The patient becomes symptom free in another twelve hours. According to Stokes, Beerman and Ingraham,¹³ this reaction occurs in 20 per cent of patients with late syphilis who are treated with penicillin. It may be grave, as is evidenced in the report of Lentz and his group,¹⁴ who observed threatened abortion in 2 pregnant women treated for early syphilis with penicillin. This occurred within eighteen hours after the beginning of treatment in one case and within forty-eight hours in the other. The drug was discontinued immediately but was resumed in full dosage in twenty-four hours, without recurrence. Lentz et al believe that this type of Herxheimer reaction may be referred to as "placental shock." In another article, Ingraham and his associates⁵ report that a patient with early latent syphilis in the fourth month of pregnancy aborted on the fourth day after the beginning of penicillin therapy. In this case, treatment was begun cautiously, with a low dosage of penicillin for the first three days. Goodwin and Moore¹⁵ do not agree that the reaction was due to penicillin.

Leavitt¹⁶ noted that of 21 pregnant patients treated with penicillin, 8 manifested symptoms of uterine activity, consisting of uterine cramps or bleeding, or both. In 2 cases, evacuation of the contents of the uterus occurred. In Beerman and Ingraham's⁴ series, a patient had a miscarriage during the course of treatment, and in another case, it was necessary to stop treatment until the symptoms of threatened miscarriage had subsided some weeks later.

One infant with congenital syphilis suddenly experienced severe, nearly fatal collapse forty-eight hours after treatment had been begun.¹⁰ Three infants died during or soon after treatment (twenty-four hours, seven days and nine days, respectively). All the infants were under two months of age and were in poor general condition. Two other infants died (five weeks and fourteen weeks, respectively) after penicillin therapy. Whether these deaths were due to penicillin, directly or indirectly, is not known. It is prudent, in the penicillin treatment of debilitated children, to employ considerable caution.¹⁷

The 2 cases of cardiovascular syphilis reported by Dolkart and Schweimlein¹⁸ in which anigal symptoms appeared shortly after the beginning of penicillin therapy are examples of a therapeutic paradox—a shocklike reaction that occurs at times in other vital structures, such as the liver. In all cases in which the possibility of therapeutic shock may be anticipated, it is wise to reduce the penicillin dosage by three fourths to a half for the first forty-eight hours. This reduction may be compensated for by prolongation of the course of treatment. In the present series, untoward reactions were not observed in a patient treated with penicillin who had syphilis and hypertensive cardiovascular disease and who was decompensated, or in a person who had cardiovascular syphilis with aortic regurgitation.

Neymann and his co-workers¹⁹ reported 2 fatal cases following the use of penicillin intrathecally. They stated that the route is dangerous if more than 30,000 units are injected and that the daily injection of this dose prolonged for more than five days is hazardous. Their patients who died following such treatment exhibited tenseness at first. This was followed by generalized muscular twitching and finally by severe convulsions.

In this series a patient developed postarsenical jaundice, from which he appeared to make an uneventful recovery. Three months later he returned to the hospital for study and was given 2,400,000 Oxford units of penicillin over a period of eight days. Soon, the jaundice reappeared. This was followed by a progressively fatal course. A post-mortem diagnosis of subacute yellow atrophy was made. The question whether the penicillin was responsible for death cannot be answered satisfactorily. In the presence of previous liver damage, however, penicillin should be employed cautiously if at all.

Sensitization Reactions

Only 2 patients in this series developed urticaria while undergoing penicillin therapy for syphilis. But according to Anderson,²⁰ from 2 to 5 per cent of patients treated with penicillin develop urticaria. This may appear on the first day of treatment or may not become apparent until several days after treatment has been completed. It usually develops during the second week. Occasionally, it is severe,

serologic test was reported as positive. Retreatment consisted of 600,000 Oxford units of penicillin, in addition to eight hours of fever therapy, this caused resolution of the lesions. Three months later, the serologic tests were reported negative. The lesson to be learned is that the time element (in this case, four days) is more important in cure than the total dose. The duration of penicillin therapy (four days) also appears to have been significant in Beerman and Ingraham's case⁴ in which treatment failed. In both cases the time was too short to sustain a therapeutic blood level of the drug.

LIMITATIONS OF THERAPY

Relapse

The effectiveness of a new antispirethetal agent in early syphilis is judged by the incidence of relapse, both clinical and serologic, following its use. Relapse has been defined as either a persistent, rising serologic titer or clinical evidence of progression of the disease. Its implications regarding public health are obvious.

Among 75 patients with early syphilis treated at the Massachusetts General Hospital, 2 had serologic and 3 had clinical (mucocutaneous) relapses — a rate of approximately 7 per cent in patients followed for at least six months. One of the latter group, a woman five months' pregnant with secondary syphilis, had been treated with 1,200,000 Oxford units of penicillin. At the time of delivery of a full-term, normal-appearing infant, the mother's serologic reaction was positive although tending toward negativity. The serologic reaction in the infant was negative until the third month, when it became positive. At that time, both the mother and the infant presented cutaneous lesions suggestive of secondary syphilis. From the perianal lesion of the infant, material taken for a dark-field examination revealed *Tr pallidum*. Progress after treatment with double the total dose for the mother — 2,400,000 Oxford units of penicillin — and a total dose of 1,200,000 units for the infant has been satisfactory. Beerman and Ingraham⁴ reported a somewhat similar case in which the same dose was given in four days. This patient, who had not been cured of syphilis, had an infectious relapse and transmitted the disease to the infant about the time of delivery.

In a group of 27 pregnant women with early syphilis who were treated with penicillin by Ingraham and his co-workers,⁵ the rate of clinical and serologic relapse was 11 per cent.

Moore⁶ reported that the incidence of relapse when penicillin was administered alone was in direct relation to the total dose given by the intramuscular route in a period of seven and a half days. It was greatest with 60,000 units and least with 1,200,000. Relapse appeared to be more frequent after intravenous use than after intramuscular administration of comparable doses.

In a report by the Committee on Medical Research and the United States Public Health Service⁷ on the treatment of early syphilis with penicillin, the lowest cumulative failure rate — 15 per cent at the end of eleven months' follow-up study — occurred following the administration of a total dose of 2,400,000 Oxford units. With a total dose of 60,000 units, the rate was 62 per cent.

In a series of cases of early syphilis reported by Moore et al.,⁸ patients with seronegative primary syphilis treated with intramuscular penicillin showed a relapse rate of 3.2 per cent. The rate was 5.0 per cent in those with seropositive primary syphilis, and 9.8 per cent in those with secondary syphilis. Leifer⁹ reported that 96 patients with early syphilis treated with a total of 1,200,000 Oxford units had a relapse rate of 9.6 per cent. Leifer's series also included 2 patients who had neurologic relapses. Although the seriousness of this complication was appreciated, it was not encountered in the series at the Massachusetts General Hospital.

The lowest incidence of relapse⁸ and the most favorable serologic response was seen in a small group of patients treated with 60,000 and 300,000 Oxford units of penicillin, together with a known subcurative dose of Mapharsen. Similar results have been reported in patients treated with penicillin and bismuth.⁷

Observation of 69 infants treated for infantile congenital syphilis revealed serologic relapse in 5 patients, with clinical relapse in 2 of these cases.¹⁰ Serologic relapse occurred in three to six months after treatment, and clinical relapse at six months.

Serologic and clinical relapse in the cases of early syphilis in this series was noted between the third and the ninth month, but the danger period extended to the end of the second year following the original treatment.

Reinfection

Reinfection as opposed to relapse is infrequent. Of 150 supposed reinfections, clinicians associated with the Central Statistical Unit agreed to fulfillment of adequate criteria of reinfection in only 2 cases.⁷

Although one case failed to fulfill these rigid criteria, it portrayed a frequent pitfall referred to as "pingpong syphilis" (Schoch and Alexander¹¹), which occurs uniquely in penicillin-treated syphilis. A male patient was discovered to have a dark-field-positive chancre, for which he was given 2,400,000 Oxford units of penicillin intramuscularly. A month later, his wife developed a vulvar lesion. Her serologic reaction at that time was positive, but no dark-field examination was performed. Early in the next month she received 2,400,000 Oxford units of penicillin intramuscularly. Three weeks later the husband noted a penile lesion on the opposite side from the original chancre. Dark-field examination was negative at that time but was reported positive for *Tr pallidum* a month later. It is reasonable to believe that the husband after infecting his wife was cured.

this treatment can be obtained. They are instructed to present their separation-report leaflet to the physician of their choice, informing him that the type, amount and dates of treatment are on file at the state health department. This leaflet shows the results of serologic tests, including a report of the examination of the cerebrospinal fluid taken before discharge from the service. The treatment these patients have had is listed on Form 78A. If for some reason this form is not obtainable from the state health department, or if further information is desired, the physician can write to the Bureau of Medicine and Surgery, United States Navy, or to the Preventive Medical Service, Office of the Surgeon General, United States Army, in Washington. With this information at hand, the attending physician should be able to reach some decision on future follow-up study of the patient.

At the Massachusetts General Hospital, patients with early syphilis who have been treated with penicillin are seen for follow-up examinations (including at each visit a complete physical examination, with special attention to the skin and mucous membranes, and a quantitative serologic test) every two weeks for the first year. At the end of the first year, if there has been no clinical relapse and serologic tests are negative, another examination of the cerebrospinal fluid should be made. During the second year, the patient should be seen at least every three months. Attention is again called to clinical and serologic relapse, which is most frequent in the first two years after the initial treatment for early syphilis. At the end of the second year, assuming that all findings are negative, the patient is placed on a yearly follow-up basis for the remainder of his life, the wisdom of programs that advocate following the treated veteran for a maximum of only five years is doubtful. Again, assuming that the patient is progressing satisfactorily, an examination of the cardiovascular system, including roentgenology and fluoroscopy, is made five years after treatment has been completed. This entire subject, together with the action taken on it by the armed forces and civilian public-health authorities and with the part the civilian physician and the veteran himself play in it, has been reviewed in detail by Perkins.²⁴

It is further realized that men and women returning from the service have a responsibility in this program that they may, for various reasons, choose to neglect. Although proper methods of handling this situation exist in the state and local departments of public health, the private physician is lost when the patient fails in his duty. In certain states and communities, however, the private physician can, by communicating with the department of public health, by telephone or in writing, obtain the services of a trained social worker in venereal disease, who will get in touch with the lapsing patient. In this

capacity, the social worker acts as the private physician's confidential representative, urging the patient to continue under the care of his physician. Persons failing to respond to this approach should be reported to the proper state or local public-health department for more aggressive action.

Marriage

When should a person who has had early syphilis and who has been treated with penicillin marry? My policy has been to advise postponing marriage until two years after the blood serologic reaction had become negative, provided that during this interval the patient is free from clinical manifestations and exhibits a persistently negative serologic reaction. At the end of this probationary period a spinal-fluid test must also be negative. Anything short of this regime invites disaster.

SUMMARY

Although many of the untoward results of penicillin therapy will be remedied as experience with penicillin increases, especially when more studies become available in which various combinations of other antisyphilitic drugs are used in conjunction with penicillin, therapeutic overenthusiasm on the part of the practicing physician must be tempered by the facts presented above.

It is the duty of the physician who treats syphilis to know the types of the disease in which results with penicillin are inconclusive, to understand such therapeutic pitfalls as lapse, relapse, resistance, reinfection and the problems of retreatment and to familiarize himself with reaction hazards. It is incumbent on him to protect the public health by encouraging the returning veteran to continue the splendid work that the armed forces have performed in the treatment of early syphilis and by advising against the ill timed marriage of patients who have been treated for early syphilis with penicillin. Finally, a high index of suspicion regarding syphilis will protect the practicing physician from unwittingly adding to the reservoir of hidden syphilis by administering treatment that may mask the disease.

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but in most cases it is mild and frequently disappears even if treatment is continued.

Another type of allergic response is a vesiculobullous or papular eruption, generally followed by desquamation. This also occurs in the first twenty-four hours. The continuation of therapy in these cases aggravates the disease.

Transient gastrointestinal reactions, consisting of nausea, vomiting and diarrhea, have been noted in syphilitic patients treated with penicillin.

The maximal dose of penicillin that can safely be given to man has not been determined. So far as is known, penicillin is not incompatible with any other antisyphilitic drug.

PUBLIC-HEALTH ASPECTS

Masking of Syphilis

In 1 case in this series the treatment of gonorrhea with penicillin during the incubation period of syphilis masked the disease. The diagnosis of syphilis was delayed for six months, and during the interval the patient infected his wife. Walker and Barton²¹ reviewed 8 cases in which patients with gonorrhea were treated with 100,000 Oxford units of penicillin—given in one day—during the incubation period of syphilis. Such a small dose of penicillin, although capable of curing the gonorrhea, is likely to suppress the primary and secondary manifestations of a concomitant early syphilitic infection but does not prevent recurrences. Under these circumstances, the patient is denied the benefit of adequate treatment for syphilis in the seronegative stage, in which the chances of cure are greatest, and the public is exposed to a definite source of infection. In most cases the patient's condition is diagnosed weeks or months later when he is seen with a clinical or serologic relapse.

Magnuson and Eagle²² stated that, with the increasing use of penicillin for gonorrhea, it is probable that the number of aborted, delayed or symptomatically acquired lesions of early syphilis will increase. MacKenzie and Wrong²³ therefore advise the use of sulfonamides rather than penicillin in cases of urethritis in which a coincidental infection with syphilis is suspected. These authors noted that penicillin administered during the incubation period of syphilis in subcurative doses modified the early bacteriologic and serologic findings. In their cases the appearance of the chancre was delayed to from sixty to seventy days, rather than the usual twenty-six days, and the serologic reaction became positive in four to five months, instead of an average of forty-five days, from the date of the infection. They also found that when the primary lesion of syphilis appeared, it was necessary to perform repeated dark-field examinations before a positive result was obtained. Therefore, it seems necessary to subject patients receiving penicillin for gonorrhea to a six months' follow-up study for syphilis. Any patient who has gonorrhea and shows an early Herxheimer

reaction,²¹ evidenced by a rise in temperature after the first injection of penicillin, should be examined for syphilis.

Another pernicious habit concerns the blanket use of penicillin in mucocutaneous ulcerations, in which such treatment may mask the coincidental development of syphilis. A patient in this series had been treated for an ulcerative genital lesion by a physician with 600,000 Oxford units of penicillin, peanut oil and beeswax mixture intramuscularly, with no attempt to diagnose the condition by dark-field examination or pretreatment serologic reaction. This treatment, which was inadequate for early syphilis, was sufficient to render the dark-field examination negative for *Tr pallidum* and probably delayed the development of a positive serologic reaction. To protect such patients and the community at large, it is necessary to accept the diagnosis of syphilis under these conditions and to offer treatment sufficient to cure.

Another case was that of a young woman with an ulceration of the lower lip who had been treated with penicillin troches. The medication caused the lesions to regress temporarily, but several weeks later, when the diagnosis was suspected, a dark-field examination revealed *Tr pallidum*. A serologic test taken at that time was positive.

Lapse of Treatment

In general, experience with this group of patients revealed that case holding is far more difficult for penicillin-treated early syphilis than for patients treated under the arsenic and bismuth regime. Under the latter, the patient is satisfied that something positive is being done at each visit—namely, treatment. On follow-up study after penicillin treatment he is merely "looked at" and blood is drawn for a serologic test. This circumstance, together with the early favorable reports of the test, lulls him into complacency. One of the great advantages of the arsenic and bismuth regime, from a public-health viewpoint, was that patients with early syphilis received some treatment continuously during the first year and a half or two years of the disease, the time of greatest relapse.

The Returning Veteran

High on the list of problems in public health in the treatment of syphilis with penicillin will be the follow-up and case-holding system for the returning members of the armed forces who have been treated for syphilis with penicillin while in the service. The family physician will undoubtedly share in this aspect of the problem. He should therefore be acquainted with the following facts, if his patient and the community are to be protected.

All service personnel who have been treated for syphilis while members of the armed forces are informed before discharge what is expected of them in following up their treatment and are told where

considered from an economic rather than a medical standpoint

Another aspect of medical care is that of public health and preventive medicine. Half the counties in the United States do not have a full time public-health service. In other sections the department of public health is under political control, and there is no efficiency of administration. It would not be feasible, of course, for every county in the United States to have a full-time public-health department. Indeed, there are five counties in the United States with only five persons per square mile, they could not afford it and would not need it. But neighboring counties could join and form a district health department, with a traveling health service. This could be done in most states within their own economy. If state funds are lacking, there is a legitimate opportunity for the federal government to help, leaving the control of the situation in local hands.

It is much better to prevent disease than to cure it after it has started, and the control of many diseases is dependent on the quality of public-health facilities, of sewage and mosquito control and of water and milk supplies. Some of the diseases can be entirely eliminated by proper public-health measures. Again, there is no necessity for pouring in medical care.

The shortage of physicians in certain areas is widely discussed. The doctor does not settle in a certain community primarily because there are not facilities for him to bring up his family and educate his children, or for competent practice. He has been trained to practice a high type of medicine, and when he goes to a community and finds no adequate facilities he either leaves or remains and practices poor medicine, which is even worse. The solution is the provision of hospital and diagnostic facilities in these areas. That approach is the main substance of the Hill-Burton Bill in Congress — providing such facilities throughout the country where they are not now available, the states retaining control over these institutions constructed with federal money. In some areas the lack of medical care will thereby, to a certain extent, be solved, in others it may be necessary to provide a subsidy for a physician to go to an area because of the small number of patients to be cared for. This problem can be solved through voluntary agencies.

Medical care has become more expensive, I believe, primarily because of the increased science that has developed. Seventy-five years ago, medicine was not a science but an art, it is now an art, as well as a science. There are those who wish to throw the art out the window and make medicine 100 per cent science, but the result would not be satisfactory. There is still the individual touch in medicine, as well as the effect. You men know, as well as anybody in the world, that the treatment in two cases of pneumonia cannot be identical merely

because the diagnosis is the same. Psychology is involved in the treatment of every patient — in the so-called "doctor-patient relation," which is one of the reasons for the success of the American system of medicine, preventing the doctor from being exclusively scientific and the patient from being merely a case number.

The increased expense is not so much in the care that the physician gives — he is paid little more than he was a generation ago for a house call or an office visit, the cost is in diagnosis. The doctor must have expensive pieces of apparatus, as well as complicated procedures, to practice competent medicine today. He must have equipment for x-ray films, electrocardiograms, blood chemical studies and so forth, all of which cost the patient money. It is those matters that need attention and whose solution will be aided by some such means as the Hill-Burton Bill.

One other important measure is in insurance, about which a good deal is heard at present. You are all familiar with the proposal now before Congress, with hearings before the Senate Subcommittee on Education and Labor, the Wagner-Murray-Dingell Bill calling for compulsory health insurance. Organized medicine has sponsored a voluntary program. Certain members of the committee, Senators Murray, Wagner and Pepper, assert that the voluntary system will not work. They cite reasons, every one of which is susceptible of overturn. America is undoubtedly the best insured nation in the world, from every aspect. The American people are insurance minded, but they must be sold on the idea of insuring their health. I understand that it took fifty years to make the idea of life insurance successful. I do not mean to intimate that it will take fifty years for voluntary health insurance to succeed. In those days, nobody knew anything about the types of insurance that could be obtained. At present, it should be comparatively simple to sell health insurance, but it must be made available.

There are two types of hospital insurance — that provided by the Blue Cross and that sold by various commercial companies. The Blue Cross alone has somewhere around 22,000,000 people insured, and the number is going up week by week, in fact, every time I speak on the subject I have to amend the figures, so that I am not sure that 22,000,000 is correct at the present time. And there are many more who are insured for hospitalization through insurance companies.

Then, too, people are carrying all sorts of health and accident insurance. Probably 30,000,000 in the United States have some form of protection against illness. Not all of it is the same. Some of it is complete, and some of it covers emergencies; some of it covers surgery and obstetrics, and some of it covers hospital and medical care, some of it is commercial insurance, some of it is industrial insurance,

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THE MEDICAL-CARE PROBLEM IN THE UNITED STATES*

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I SUPPOSE that there is no problem quite so controversial in the United States as that of medical care. We hear a great deal of propaganda—in its modern connotation, not its original one. It is not information, it is information on one side, an attempt to sway people into changing their opinions, regardless of facts. The medical profession and the whole subject of medical care have been the object of considerable vicious propaganda of that order for the last several years.

It is quite true that medical care in many areas of the United States is not what it should be, and that it is susceptible of a great deal of improvement. Many things that are said about it, however, are definitely not true. Of course, those things are said with the idea of deluding the public, so that they will accept something quite foreign to the American idea of how things should be done.

One of the subjects most frequently discussed is the matter of Selective Service statistics. It is constantly stated that these statistics showed that American manhood is falling apart. The facts are that although 4,217,000 men were rejected, 582,000 of those were rejected for mental deficiency, including 250,000 illiterates, and about 701,000 for neuropsychiatric defects. The psychiatrists would be the first to admit that those men could not have been made fit for medical service, no matter how much medical care they received. Furthermore, out of the total number, there were those who were totally blind or totally deaf, as well as those without an arm or a leg.

Therefore, when the statistics are analyzed down to the last man, it is found that not over 15 to 20 per cent, and probably not even that number, could have been salvaged for the armed forces with any

medical care. Most of those rejected who were given an opportunity to have the defects corrected refused. Furthermore, people fail to consider that the medical standards of the United States Army and Navy were the highest in the world. Men rejected by our forces crossed the line into Canada and were accepted. No one would say that the cadets at West Point and Annapolis were in poor physical shape. Yet the fact remains that not more than 40 or 50 per cent pass the physical examination for flying.

Many other charges are made that do not concern medical problems at all. For example, as I have pointed out before, there was a cartoon several years ago showing a woman in rags and a sad state of malnutrition, surrounded by children in a similar condition, and the cartoon was entitled, "These people need medical care." That was used as propaganda to overturn our system of medical care in the United States. The people portrayed needed a great many other things worse. If they had been properly clothed and housed and fed, they probably would have needed little medical care. The problem is really economic, it becomes medical because of the economic factors, and all the medical care in the world will not solve the problem. The cure of the evil is an economic one, which is the community's responsibility and not primarily that of the medical profession.

One of the points of the American Medical Association program is that people should have proper housing, clothing and food, and that they should obtain these on an individual basis whenever possible, when it is not possible—for example, if they are misfits in the community—the community must take care of them, and so on up to higher levels if the local resources are inadequate. Thus, again, a certain section of the population that is in need of medical care is eliminated if the problem is

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Even Mr. Altmeyer, in his cross-examination, had to admit that the choice was limited. He also said that if the physicians in a community did not agree to serve under the plan, the Public Health Service would send doctors into the area to practice medicine. That is how much the free choice amounts to.

The statement is also made that organized medicine is unfair when it claims that this is the first step in national socialization. A glance at the background is sufficient. What happened in Germany? The Germans had compulsory sickness insurance. What is happening in England? They are socializing all their public utilities, even the Bank of England. In 1938 or 1939, the year that the American Medical Association met in Atlantic City, a senator from Illinois came directly from Washington and asked permission to speak to the House of Delegates. That was granted. He made the following statement:

We know nothing of patient, don't recognize its existence. It is your creation. We recognize an instrument called citizen, who is essential to the welfare of government.

Most of us were brought up to believe that the state was for the welfare of the citizen. One can find similar words about the citizen and the state in *Mein Kampf*, and yet the senator's statement has never been denied by anybody in Washington.

There are other shortcomings in the Bill. Compulsory insurance will be extremely expensive, the medicine provided will be anything but free. This Bill does not mention how the money is to be raised. That, of course, was done for a specific purpose to get the bill into the hands of Senator Murray's committee. If taxes were mentioned, it would have to go to the Finance Committee, of which Senator George is chairman, where it probably would have received a frosty reception.

The money will have to be raised somehow. President Truman mentioned a 4 per cent tax, up to \$3600, for each employed member of the family. If two people in the family received \$3600, they would have to pay \$288 for medical care. That is an extreme case, it may be said, because many people are in the lower income brackets. But that is not necessarily making the outlay of a family smaller, because when there are more people in the same family working, then the net cost will be higher. It is estimated that approximately four billion dollars, which is stated to be the present cost of medical care in the United States, can be raised by taxes. In my opinion, fourteen billion dollars would probably come nearer the actual figure if such a vicious scheme as this were adopted. We do not know how many bureaucrats would be given jobs if the bill went into effect, but at least 300,000 to 400,000 would undoubtedly be employed. In England, they have two nonmedical employees to one physician, and, in the extravagant way we do things in this country, there would probably be three or four to one. That army of people would

have to be taken care of before any poor patient got a doctor. Inspections would be necessary everywhere. A bureaucratic government cannot be run without red tape — it thrives on it. The experiences of the depression should be remembered. In New York the Emergency Relief Administration prescribed regulations whereby doctors had to ask permission to visit a patient. They could go and make an initial call, and whether they got paid for it or not, they had to estimate the number of calls necessary for them to make on that patient, as well as giving the diagnosis on the patient, all the information being submitted on a postal card, mind you. If they found that the patient had complications, they had to get extra permission for three or four more calls. They were also told what to prescribe and what not to prescribe. Certain things were too expensive, and the government clerk was the one to prescribe, not the doctor. All these up-lifters say that no interference in the practice of medicine is intended in the bill. Why was there interference by the Emergency Relief Administration during the depression? We can expect nothing different. It will be the same thing, only more so. It is simply the initial attempt on the part of a certain group to make this a totally socialist government. The next step will be easy.

There are one or two other matters in this bill that I should like to mention. A so-called "advisory council" is emphasized as being quite important. It will have sixteen members, I believe, who are to be appointed by the Surgeon-General of the Public Health Service. These names must be selected from panels submitted by professional and other societies. But the board has no authority. It is advisory only. Furthermore, do you think for one minute that the Surgeon-General will appoint to the board people he knows are going to disagree with him? Of course not! That board will be a sounding board, that is the only relation that it will have to a "board," in my opinion. Local boards in the various states and communities will actually run the practice of medicine.

It is all very well to say that this is not socialized medicine, that the patient will have free choice and that people will get medical care that was not previously available. It is socialized medicine. Some people may get medical care that they have never had before, but it will be inferior. In all countries where the government has taken control over the practice of medicine, the medical care has deteriorated.

Senator Pepper said that he wished the people would get as stirred up about the 600,000,000 man-hours lost from ill health as it did about the hours lost by strikes. It might be well to consider what has happened in other countries in that regard.

When compulsory insurance was developed in England, it was expected that the sickness rate would go up initially, because people would go to

and some of it is carried in the plans sponsored by the medical societies. It is interesting to note that there is an increase of 114 per cent in the number of people insured under the last system alone, which shows that this idea is growing. It has been slow, of course. And that is one thing that must be admitted when the voluntary program is attacked. But I think that it is wise to go slow.

The American Medical Association was roundly censured in many quarters when the first approval was given to voluntary medical insurance because many people believed that the American Medical Association should advance an overall plan covering everybody in the United States. Nobody knew what was wanted. There was no actuarial background. No one knew how the medical profession or the public would react. Consequently, if a plan were developed and sold over the United States, the thing would have been killed years ago, it could not have worked. Accordingly, it was considered better to experiment and to start in small areas, accepting what was good and rejecting what was bad. There has been experimentation over a period of years, and we are beginning to know what is acceptable and what is not acceptable. As a result, order is beginning to come out of chaos, and, as you probably know, the American Medical Association has just established a Division of Prepayment Medical Care and Insurance in the Council on Medical Service at headquarters in Chicago, and there has been formed an independent organization, Associated Medical Care Plans, which takes in all the plans that sell insurance, provided that they meet certain specifications set up by the Council. The idea is to make these plans uniform, so far as possible, and to have reciprocity among them so that a person moving from one state to another will not lose his insurance but may transfer to the plan in another state. Organizations having a national payroll with employees in New Hampshire, Massachusetts, New York, Pennsylvania and other places do not have to go to half a dozen different places to insure employees. They can go to one central agency, where they may be insured in different organizations. General Motors Corporation, for example, is not willing to insure its employees in New Hampshire for medical care if it cannot do the same thing for its employees in another state. It is essential that these plans be available nationally, and some arrangement should be made whereby they can be sold nationally, even though they are actually sold by different companies.

Another criticism leveled at voluntary health insurance is that few of these plans give complete medical care. That is true. The reason is that most of the plans that started out with complete coverage were unsuccessful because the public was not interested in an illness of three, four or five days, they are interested in the expensive type of illness and hospitalization, such as operation or

delivery. That type of insurance is incorporated in most of the plans, and many of them are adding medical care in the hospital—that is, the patients are protected for surgery, obstetrics, and if they have an illness that requires hospitalization they are protected for the medical care while in the hospital. It has been interesting, in New York, at least, to note that the people who have been carrying limited insurance say that this increased policy for medical care in the hospital can be sold to holders of surgical and obstetric insurance much more easily than to people with no insurance at all. In other words, the former have become more insurance minded. They see the benefits and want to extend them. The policy that will ultimately be more or less universally sold will probably cover surgery, obstetrics and medical care in the hospital. Eventually, complete medical care in the office and the home may be included, but that will take time. That is the least important, because the greatest part of the problem will have been solved if the economic situation is improved, if diseases are controlled and eliminated by proper preventive medicine and public facilities, adequate diagnostic aid and hospital facilities and if protection against the costs of surgery, obstetrics and hospital medical care is provided.

The Wagner-Murray-Dingell Bill proposes a system of national health insurance, and we are told that this is not socialized medicine. In fact, I believe that President Truman, in his message on health, made that statement about five times, I do not know how many times Senator Wagner made the same statement when he was discussing the introduction of his bill to the Senate. "Methinks, the lady doth protest too much," as Shakespeare said. It certainly approaches socialized medicine, it is political medicine, anyway, which is worse. The Government collects the money and pays it out. The Government prescribes the regulations under which physician and patient must act, determines who is a specialist and, in certain instances, even decides who can have a specialist. That part of the bill pertaining to specialists states that the practitioner in charge of the case may summon a specialist, and the patient has no voice in the choice of the specialist. If the patient desires a specialist, he can make application to the nearest governmental agency for the specialist.

Senators Wagner, Murray and Dingell say that there is a free choice of physician. It is a free choice, if the physician agrees to take part in the plan, but not otherwise. Also, a physician can be chosen provided that his panel is not already filled, for the Bill limits the number of patients that a doctor may have. It is free choice, provided that the majority of physicians do not elect to be paid on a capitation basis. I see no possible way of having that without allotting people in a certain area to a certain doctor, which would not be free choice.

RECENT ADVANCES IN THE CARE OF THE SURGICAL COMPLICATIONS OF DIABETES MELLITUS*

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BOSTON

MUCH has already been written on the factors involved in the care of the surgical complications of patients with diabetes mellitus. The purpose of this paper is not to review the entire problem but rather to consider the effects of many recent advances in medical science on the care of these patients. I shall confine my remarks to the consideration of the surgical problems.

It is difficult to evaluate the factors that have improved the care of poor-risk and elderly patients in recent years. The security of all patients undergoing surgical procedures has been aided immeasurably by more careful and deliberate preparation for operation, an increasing understanding of fluid balance, parenteral feeding, including the vitamins, whole blood and plasma transfusions, the use of intestinal antiseptics in preparation for resection of the large bowel, and early mobilization. These benefits are shared alike by patients with and without diabetes. It should never be forgotten, however, that the diabetic patient must be evaluated in terms not only of his general and local surgical condition but also of the diabetic state and the facilities at hand to control it before and especially after operation. Increasing experience has convinced me that diabetes mellitus is no contraindication to any surgical procedure whose indications are clear, provided always that the medical, surgical and hospital teamwork is such as to ensure efficient, co-operative care of the patient's metabolic disturbance.

If possible, surgical emergencies are to be avoided. In a patient whose general condition permits the procedure, an operation for gallstones, interval appendicitis, hernia and the like is advised as soon as it can be done under conditions likeliest to assure a safe convalescence.

This discussion chiefly concerns two conditions that are not limited to patients with diabetes but that present particular problems to such patients — operations for which account for over two thirds of the surgical procedures carried out on the diabetic patients at the New England Deaconess Hospital. These conditions comprise infections of the skin and subcutaneous tissue, especially carbuncles, and gangrene and infections of the lower extremities. It is gratifying that the medical advances of the past five years have proved particularly helpful to patients with these complications.

Carbuncles

The 7 deaths among the 95 patients with carbuncles operated on between 1928 and 1941 give no concept of the seriousness of this problem in terms of loss of time and suffering of the patient. It is too early to evaluate the full benefits that penicillin in adequate dosage offers to the patient with a carbuncle. Experience to date at the New England Deaconess Hospital, however, has been most gratifying. We have seen the large, brawny, indurated, painful lesion characteristic of the earlier stages of a large carbuncle completely disappear after control of the diabetes and the daily injection of 100,000 to 300,000 units of penicillin for seven to ten days. Similar lesions in a more advanced stage have resolved into small local painless fluctuant areas 2 or 3 cm. in diameter and have healed promptly after local incision; these lesions, at the worst, would have resulted fatally in 5 to 10 per cent of cases prior to the use of penicillin and, at best, would have cost the patient weeks of hospital care, as well as a wound requiring months for final healing.

To date the cases have been too few and the experience too limited to warrant any definite conclusions. It is adequate, however, to establish a working basis for the management of this type of lesion.

On the basis of this experience any diabetic patient with an early carbuncle is regarded as an emergency and is immediately admitted to the hospital. The diabetes is carefully treated, and daily injections of 300,000 units of penicillin are given in eight equally divided doses until the lesion is operated on or has resolved.

It is to be expected that the greater part of the cellulitis will either disappear completely or leave a broken-down central area that is probably best treated by a small incision, release of the fluid, packing with gauze for twenty-four to forty-eight hours and allowing the skin edges to fall together. This method of handling the small residual cavity has in this limited experience been more satisfactory than attempts to control it by aspiration.

It is quite possible that the small carbuncles that fail to resolve completely and in which necrosis of skin occurs are best treated by excision and early skin graft. If the experience of the past two years is any guide for the future, the extensive operations for large carbuncles previously seen will seldom, if ever, be necessary, except in the badly neglected case.

*From the New England Deaconess Hospital. Presented at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1946.

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a doctor who could not have afforded it previously, and that the costs would be increased for a while. Then the rate was expected to come down, because the patients would go to a doctor earlier, would not be sick so long and many conditions that they might otherwise have had would be prevented. The rate never did come down, however—in fact, it is still going up. Why? Because it encourages malingering. The number of man-days lost in the United States is 9 per man. In England, before the compulsory sickness insurance went into effect, it was approximately 11, it is now between 14 and 15. In Germany, before compulsory sickness insurance was adopted, it was around 14, and it went up to 28. Consequently, the problem of man-hours lost will not be solved by compulsory sickness insurance, it will be increased rather than decreased.

We all want more medical care, but we want it to be of a high quality. We believe that the program of the American Medical Association, which was released in February, is going to solve that.

The economic aspect of medical care was discussed above, as were preventive medicine and public-health service. Increased aid to the prospective mother is also a necessity. Adequate care in childbirth and proper nutrition to prevent disease in the child should be available on an individual basis, and if the patient is unable to pay for it, help should be given on a community basis, with Federal aid, if necessary, the doctor-patient relation being preserved.

Another point is a proper program for the veteran. I am glad to say that the present officials of the Veterans Administration are anxious to see the veteran taken care of in his own community by his own doctor, and that so far as possible, they are endeavoring to complete this program. They have already worked it out in several states, and they are now in the throes of making arrangements with New York, I hope that you will do the same here—that is, that you will make arrangements with the Veterans Administration on a reasonable basis to both sides, so that the veteran can be taken care of by you in his own community and not be sent to a public institution, unless he has some chronic disease.

Another point is that of research, which, it is generally agreed, should be extended. We are perfectly willing to have Government aid in the matter of research. We want it controlled by a scientific board, and not by a politically appointed director. One should not forget the aid given by the various philanthropic associations, such as the National Tuberculosis Association and the National Foundation for Infantile Paralysis, all of which are per-

forming an excellent service and whose work would be cut off by any national program, making it that much more expensive, because those agencies did it purely on a voluntary contribution basis. One improvement could be made: the organizations should not have a dozen drives each year but one drive for all of them, the money being divided in the proportion actually needed.

Another important factor is education. By education, I mean that not only of the public, but also of the doctor, who is often not informed in these matters. If the average physician is asked whether he is against the Wagner-Murray-Dingell Bill, he will say "Yes." But, if he is asked why, he cannot explain. But physicians must know why they are against it, because the patients are interested. After all, the patient is the one who will decide whether or not the United States is to have socialized medicine, the medical profession will not decide the question. And, the public will get what it wants in the long run. But I cannot believe that the public knows what costs are entailed and what poor medical service will be provided under the proposed national health legislation. And you, gentlemen, must be the ones to tell them about it. Often, the public is not even aware of the facilities that are available.

During the hue and cry when the first Wagner-Murray Bill was introduced, the Medical Society of the State of New Jersey, asked, by way of radio, public speakers and the press, that any person in New Jersey who could not obtain medical care communicate with the Society or one of its county societies, the care being guaranteed. There were only 127 people who said that they could not obtain adequate care, and every one of these could have obtained medical care but did not know how. It is therefore a matter of educating the public of the ways available.

A fact that I have stressed many times and shall continue to stress is that there should be more interest in the county societies. I do not know the situation in New Hampshire, but if it is like that in the rest of the country, the county society is not active and the meetings are poorly attended. It is highly essential that the county society be the activating force in all these matters, otherwise, we are defeated before we start. The physician must be the engine in this whole matter, and he needs the backing of his county society. We must stimulate interest among the members of the medical societies to come out and take an active part and study these questions and know what they are all about, so that when they are called on to discuss them publicly or with the patient individually there need be no fear of what the result will be.

patients (Fig 1) The importance of penicillin in the control of infection in this group is suggested when one realizes that, in routine cultures taken from 75 patients in this group, *Staphylococcus aureus* was present in pure culture in 11 cases or in com-

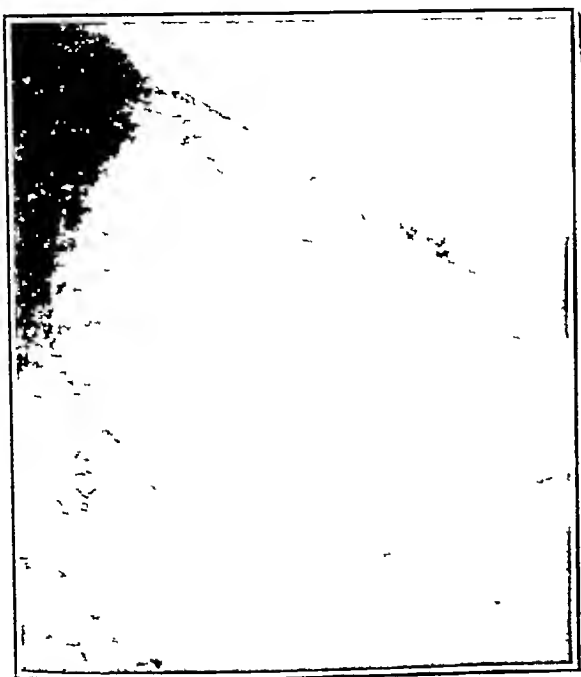


FIGURE 1 Transmetatarsal Stump Nine Months after Amputation for Gangrene of the Third Toe

There was no dorsalis pedis pulsation, but an excellent anatomical and functional result was obtained. Note the long plantar and short dorsal flaps.

bination with other organisms (usually one of the streptococci) in 41 cases

The first transmetatarsal amputation was done in March, 1944. Between then and May 1, 1946, such operations have been performed in 75 cases. Eleven of these were failures, and 1 patient died of coronary heart disease following a higher amputation. The indications for this procedure are not yet completely clear, and in certain cases a small area of necrosis on the dorsal flap (Figs 2 and 3), which has greatly prolonged the healing time, has been disturbing. The indications for the operation will continue to be extended until a careful follow-up study of all patients satisfactorily demonstrates a clear-cut conception regarding when it should or should not be undertaken. The factors involved in the area of necrosis mentioned above are also being studied, in an attempt to eliminate this if possible. A thorough and complete follow-up examination of the late functional results in a large series of patients is also essential before the final evaluation of this procedure can be made.

This experience, however, has been sufficient to cause the conviction that amputation at this level is practical, that with the use of penicillin it is safe that the functional result is good and that it has been and will continue to be a method that—if carefully carried out following proper preparation and under the protection of penicillin in adequate dosage—will obviate amputation at a higher level in many cases. Just how many of this group of 75 patients would have had amputation either through or above the mid-lower leg in previous years is impossible to say, but a review of the records of these patients seems to show quite clearly that at least

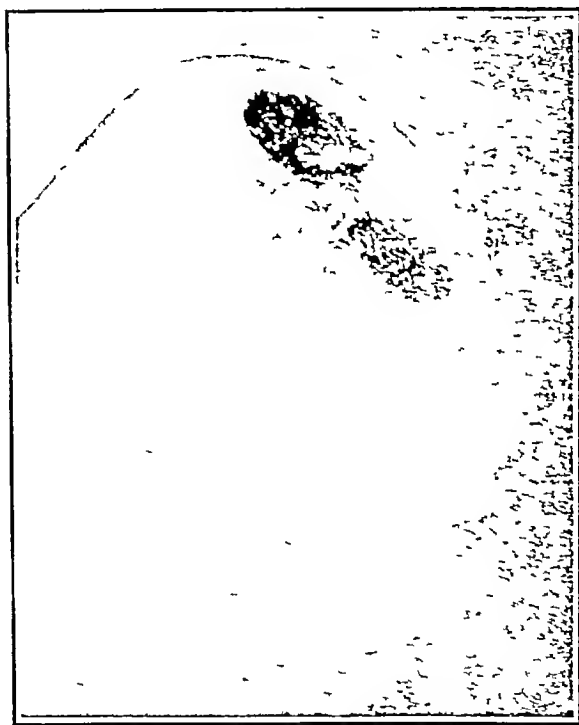


FIGURE 2 Areas of Necrosis on the Dorsal Flap of a Transmetatarsal Amputation for Gangrene of the Tops of the First and Second Toes of a Pulseless Foot

This necrosis does not involve the skin of the plantar flap and usually occurs at the site of the more lateral area.

10 to 15 per cent, probably more, of this particular group would have had a major amputation prior to the use of this procedure.

One further improvement in technic should be mentioned. Formerly, when amputation of a digit with the head of its metatarsal was carried out for an infected joint, it was the custom to leave such a wound widely open. This large open wound required weeks, sometimes months, to heal, and in many cases the resulting scar was not good. This was especially true when the foot had been split for removal of the second, third or fourth toe with its

At present the hospitalization of every patient with a carbuncle is strongly favored, with the parenteral use of penicillin rather than local injection or oral administration

Leg Lesions Requiring Major Amputations

In 1934 McKittrick and Pratt¹ carefully analyzed the 57 deaths that had occurred at the New England Deaconess Hospital following operations for lesions in the lower extremities in 622 patients with diabetes mellitus. At that time it was suggested that if some means could be found to control the ever-dangerous infection, the mortality following amputation for gangrene should approximate 5.3 per cent. In the series of operations done between 1923 and 1942 the mortality after amputations through or above the mid-lower leg in 609 cases was 14.1 per cent, whereas that following major and minor amputations in 1036 cases was 9.7 per cent (Table 1). It is interest-

TABLE 1 *Amputations of Lower Extremity in Diabetic Patients (1923-1941)**

OPERATION	NO OF CASES	NO OF DEATHS	MORTALITY %
Amputation of one or more toes	356	8	2.2
Amputation of one or more toes, followed by major amputation	71	7	9.9
Amputation through or above mid lower leg	609	86	14.1
Totals	1036	101	
Average			9.7

ing to compare this with the results during the past five years when these patients had the benefit of the sulfonamides and of penicillin (Table 2).

It is gratifying to note the drop in the mortality after all amputations, from 9.7 per cent to 2.6 per cent, and to observe how closely the mortality of 4.7 per cent for major amputations approximates that of 5.3 per cent suggested ten years

TABLE 2 *Amputations through or above Mid-Lower Leg (1941-1945)*

YEAR	NO OF CASES	NO OF DEATHS
1941	42	1
1942	46	4
1943	44	0
1944	37	2
1945	43	3
Totals	212	10 (4.7 per cent)

previously. This remarkable improvement is considered to be of particular significance, since during this period there have been no important changes in the surgical management of these cases, except those made possible by an increasing ability to eliminate infection as a deciding factor in the type of operation to be carried out. The surgical technic, the

principles of amputation, the anesthesia and to a large degree the personnel* have remained unchanged.

We continue to favor the supracondylar amputation, which is regarded as the easiest, safest operation and the one likeliest to heal promptly without complications. Amputation through the lower leg and the Gritti-Stokes operation are reserved for selected cases. Guillotine amputation through the lower leg for patients in poor condition and with extensive spreading infection is now rarely required because of the effectiveness of penicillin.

Lesions of the Feet Requiring Minor Amputations

The improvement in mortality is not the only benefit that these patients have derived from penicillin. In previous years, experience had repeatedly shown the dangers of carrying out local operation through or near an area of infection in a pulseless foot with poor collateral circulation. It was also apparent that a closed amputation carried out above the infected area usually resulted in satisfactory healing, even though there was little apparent arterial supply at the level of the incision. It therefore seemed only reasonable that if invasive local infection could be eliminated, many more conservative operations could be carried out with safety and with a reasonable chance of success.

The sulfonamides gave protection against certain streptococci but seemed of little help in eliminating the hazards of the more frequent staphylococci. It was therefore not until early 1944, when penicillin

TABLE 3 *All Amputations (1944 and 1945)*

OPERATION	NO OF CASES		NO OF DEATHS	
	1944	1945	1944	1945
Amputation of one or more toes	64	36	1	0
Transmetatarsal amputation	13	36	0	0
Amputation through or above mid lower leg	37	43	2	3
Totals	114	115	3	3
Grand totals	229		6 (2.6 per cent)	

began to be available, that it seemed quite possible that operations could be carried out on certain of these patients with reasonable assurance that the site of amputation could be chosen on the basis of arterial supply alone.

In the group of patients operated on in 1944 and 1945 it will be noted that an operation not mentioned in the previous tables is now frequently carried out (Table 3). This amputation, just proximal to the heads of the metatarsals, is made safe and practical only because virulent invasive local infection and septicemia can now be eliminated from the complications previously so serious for these

*All operations have been done by me or my former and present associates—Drs. T. C. Pratt, R. Warren, C. C. Francis, F. W. Moore, N. J. Wilson and J. B. McKittrick.

MEDICAL EXPERIENCES WITH AMERICAN TROOPS IN THE PACIFIC*

With Remarks on the Diagnostic Value of Sternal Puncture in Malaria and on the Innocuousness of Hookworm Infection

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BOSTON

THIS report is based on patients seen during two years at a large United States Army general hospital in the rich Lockyer River Valley of southern Queensland, seventy miles west of Brisbane, Australia, and during a year and a half of service with another general hospital located first at Lae, on the Huon Gulf in northeastern New Guinea, and later at San Fernando, at the upper extremity of the Lingayen Gulf, Province of La Union, on the Island of Luzon, in the Philippines. Many of the observations made were new to us as individuals, others, to the best of my knowledge, are new to medicine. Alert medical officers, depending on their special interests or training, were able to make crucial observations of certain phenomena of disease, proving some ideas and disproving others. For example, one of my colleagues — a researcher on cancer in peacetime — was able to disprove the idea long held, that betelnut chewing is carcinogenic.¹ A host of other critical observations, by-products of war experiences, will almost certainly come to light in the medical as well as in the ethnologic, anthropologic, geographic and other literature of the next few years. I am sure that many of those who have also served in the tropics could add much of interest to what I have to say about a few of the many fascinating problems met — malaria, hookworm disease, filariasis, diphtheria and scrub typhus fever.

MALARIA

When the Japanese took the East Indies they also took 90 to 95 per cent of the world's quinine. In the face of this fact and with the prospect of much tropical campaigning, the situation in the early days of the war might be described as bleak indeed. True, in the decade before the war some work had been done on the newer synthetic antimalarial drug quinacrine (Atabrine),² but that work had been carried out with native populations that had already developed, naturally, a partial immunity to malaria.

In the early days of the war in the Southwest Pacific the American forces followed a therapeutic antimalarial regimen that the Australians had found quite effective in the Middle East. Quinine was

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metatarsal head Prior to the introduction of the sulfonamides, the practice of closing the distal portion of such wounds was begun, only the proximal third or half being left open for dependent drainage. Much to our surprise, the sutured portion of the wound healed promptly in spite of the presence of active, although well localized, infection. This "re-roofing" resulted in the saving of weeks of hospital time and in marked improvement in the quality of the final scar. With penicillin, the usefulness of this procedure can be extended and the time spent in preoperative preparation can be shortened (Fig 4).

Anesthesia

Spinal anesthesia continues to be used for all operations on the lower extremities. The injection



FIGURE 3 The Same Stump Shown in Figure 2 Three Months after Revision

Note the excellent final result, as well as the use of a long plantar flap

of 75 mg of procaine crystals dissolved in spinal fluid gives excellent anesthesia of sufficient duration for any of the operations done. It is easy to use and has proved uniformly satisfactory—in fact so much so that we have found no justification for changing to the refrigeration anesthesia developed by Crossman et al.³ and adopted by many clinics throughout the country. In this elderly group of poor-risk patients no preoperative sedation is given, since it is considered to be not only unnecessary but at times dangerous.

* * *

The importance of careful preparation of patients about to undergo elective surgery is stressed.

Marked improvement in the results of the treatment of carbuncles with penicillin is discussed.

A mortality of 4.7 per cent following major amputations for gangrene or infection of lower extremities in 212 cases is compared with a theoretical rate.



FIGURE 4 Amputation of First Toe with Its Metatarsal Head for Osteomyelitis of Metatarso-Phalangeal Joint

The photograph was taken three weeks after the operation. There was excellent circulation to the foot. Note the first-intention healing of the distal two thirds of the wound, which was sutured. The proximal third of the wound on the plantar surface of the foot is not well shown. The cavity was packed loosely with dry gauze at the time of operation, which was removed three days later; it was nearly healed at the time this photograph was taken.

of 5.3 per cent suggested in 1934. A mortality of 2.6 per cent following major and minor amputations in 229 cases was made possible by the discovery of penicillin.

Transmetatarsal amputations have been done in 75 cases since penicillin became available for civilian use. 205 Beacon Street.

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MEDICAL EXPERIENCES WITH AMERICAN TROOPS IN THE PACIFIC*

With Remarks on the Diagnostic Value of Sternal Puncture in Malaria and on the Innocuousness of Hookworm Infection

HAROLD D. LEVINE, M.D.†

BOSTON

THIS report is based on patients seen during two years at a large United States Army general hospital in the rich Lockyer River Valley of southern Queensland, seventy miles west of Brisbane, Australia, and during a year and a half of service with another general hospital located first at Lae, on the Huon Gulf in northeastern New Guinea, and later at San Fernando, at the upper extremity of the Lingayen Gulf, Province of La Union, on the Island of Luzon, in the Philippines. Many of the observations made were new to us as individuals, others, to the best of my knowledge, are new to medicine. Alert medical officers, depending on their special interests or training, were able to make crucial observations of certain phenomena of disease, proving some ideas and disproving others. For example, one of my colleagues — a researcher on cancer in peacetime — was able to disprove the idea, long held, that betelnut chewing is carcinogenic.¹ A host of other critical observations, by-products of war experiences, will almost certainly come to light in the medical as well as in the ethnologic, anthropologic, geographic and other literature of the next few years. I am sure that many of those who have also served in the tropics could add much of interest to what I have to say about a few of the many fascinating problems met — malaria, hookworm disease, filariasis, diphtheria and scrub typhus fever.

MALARIA

When the Japanese took the East Indies they also took 90 to 95 per cent of the world's quinine. In the face of this fact and with the prospect of much tropical campaigning, the situation in the early days of the war might be described as bleak indeed. True, in the decade before the war some work had been done on the newer synthetic antimalarial drug quinacrine (Atabrine),² but that work had been carried out with native populations that had already developed, naturally, a partial immunity to malaria.

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scrub typhus fever and can therefore be excluded I do not know how many cases of malaria developed altogether, but the figure was probably in the neighborhood of half a million. This total provides a contrast with the situation in India, where there are a million deaths from malaria every year.

The present recommended dose of quinacrine is somewhat less than that described above. In relapsing malaria it is recommended that 1 gm be given in the first twelve hours, followed by 0.1 gm three times daily for six days and subsequently by 0.1 gm daily for two months. The veteran should be reassured that although he may have further relapses, the process will burn itself out in a year or two. The value of plasmodochin in relapsing malaria is still in the experimental stage. There is some danger in its use, but evidence is now available that it terminates relapses from vivax malaria in a considerable proportion of cases.

During the two-year period of its operation in Australia, there were 18,693 admissions to a large general hospital. In this group there were 3358 cases of malaria — about 18 per cent of the total number. This included 2222 cases of vivax, 286 cases of falciparum and 15 cases of quartan malaria, as well as 59 of mixed types and 776 of types undetermined or unclassified.⁴ Analysis of a representative sample of this material revealed many interesting facts about the symptomatology, vagaries, complications and management of malaria.⁵ Among other aspects studied was the problem of so-called "chronic malaria." In contrast to the native with chronic malaria who presents the classic picture of anemia, malnutrition and asthenia, the Army patients had complaints generally falling in four groups: neurocirculatory asthenia, symptoms referable to the musculoskeletal system, vague symptoms, such as headaches, dizziness, nervousness, insomnia and tremor, referable to the central or autonomic nervous systems, and combinations of two or more of these first three groups. Essentially, these symptoms were noted in the absence of structural organic changes. Prolonged study of these men made it clear that their symptomatology rested on a psychosomatic level. When this was recognized and the patients were treated on that basis, the treatment became more effective from the standpoint of both the individual soldier and the Army. In a much more complete study of the same problem, another group of workers⁶ found that maladjustment to the stresses of the illness and the difficulties of life in the combat hospital area played a major role in the incapacitation of the soldiers with malaria.

A standard teaching before the war was that there is no true causal prophylactic against malaria. Some of the work carried out during the war tended to refute this idea. In a group of so-called "provisional engineers," who went to Milne Bay in New Guinea in May and June, 1943, and who were de-

liberately exposed to malarial infection, a subgroup received no medication and developed malaria in 65 per cent of cases.^{7, 8} In the subgroup that received quinacrine 31 per cent developed attacks of vivax malaria when the drug was discontinued. No patients in the latter group developed malaria while taking the drug during the forty-four-day period of exposure or during the voyage back to Australia, but — and this seems particularly significant — no patient, either during the period of exposure or subsequently, developed falciparum malaria. In an Australian experiment two groups of volunteers were deliberately exposed to falciparum malaria.⁹ Twenty-six received suppressive quinacrine, begun twenty-two to forty-six days before exposure and continued for some time afterward. The other half served as a control and received no medication whatever. None of the former developed clinical falciparum malaria, whereas 100 per cent of the latter developed clinical falciparum malaria after the usual incubation and prepatent period. To use the words of these workers, "The absence of demonstrable parasites, the failure of subinoculation to transmit malaria, and the final demonstration of susceptibility and absence of premunity to the falciparum parasites injected into every volunteer, constituted a chain of evidence indicating that malarial infection had either been prevented by these anti-malarial drugs or cure attained."

A fortuitous circumstance led to an interesting side excursion in malarial research. Captain James R. Lyman had occasion to perform a diagnostic sternal puncture for possible kala-azar in an Australian returnee from the Middle East. The pathological report described, instead of the expected Leishman-Donovan bodies, plasmodium falciparum in the preparation. This surprising finding stimulated an investigation of the value of sternal puncture as a diagnostic procedure in cases in which several routine blood smears failed to show the parasites but in which the possibility of malaria was still strongly suspected.¹⁰ This study was carried out during October, November and December, 1942, with Captain Lyman and Lieutenant Harold E. Young, of the Australian Military Forces, at the 112th Australian General Hospital, where large numbers of Australian soldiers, returned from the Middle East, Ceylon, Malaya and the Indonesian Islands, presented the almost routine problem of whether malaria was present, either as a single entity or in association with some other disease.

At the time this study was interrupted by our recall to our own organization, 11 such cases had been investigated. In these cases, in which thick and thin blood smears failed to show the plasmodium, it was possible to make a definite diagnosis from the bone marrow in 7 cases (Table 1). In 3 in which the bone-marrow puncture was negative (Cases 7, 9 and 10), the subsequent course of events proved that a disease other than malaria had

produced the symptoms. Another patient (Case 8) had had malaria two years previously. Twelve thick and thin smears and the examination of sternal marrow were negative, yet quinine produced a prompt and convincing drop in the temperature. It is therefore obvious that although sternal puncture may bring to light some cases of malaria, it is not infallibly positive in the presence of malarial

precordial pain. Dyspeptic symptoms were also noted by 14 patients, but in 2 of these they were specifically related to combat and in 2 others they antedated military service. Of 34 patients treated and followed, 29 were successfully dewormed and 5 were not. Only 2 of those who were successfully dewormed were rendered free of symptoms. All the others, whether dewormed or not, continued to have the same complaints.

TABLE 1 *The Results of Sternal Puncture in the Diagnosis of Malaria*

CASE NO.	DIAGNOSIS	NO OF NEGATIVE BLOOD SMEARS	RESULTS OF STERNAL PUNCTURE
1	Benign tertian malaria bleeding duodenal ulcer	6	+
2	Benign tertian malaria	2	+
3	Benign tertian malaria	1	+
4	Benign tertian malaria	4	+
5	Malignant tertian malaria kala azar	4	+
6	Benign tertian malaria	1	+
7	Septicemia	4	—
8	Chronic malaria	12	—
9	Chronic malaria ?	4	—
10	Amebic dysentery	3	—
11	Benign tertian malaria	3	+

The second group consisted of 19 patients in the active or convalescent stage of a well defined disease with symptoms limited to those characteristic of that condition, the finding of hookworm infection was merely incidental. This group included 3 cases of infectious hepatitis, 2 of scrub typhus (tsutsugamushi) fever in the convalescent stage, 7 of various skin diseases, 2 of bronchial asthma and 1 each of bacillary dysentery, rheumatoid arthritis, urethritis, migraine and malaria. The subsequent course was typical of the particular disease presented.

The third group included 8 patients whose symptomatology was limited to the gastrointestinal tract. The symptoms comprised postprandial epigastric pain or cramping, periumbilical discomfort, a heavy sensation in the abdomen, gaseous distention and burning sensations in the stomach. Three of these patients were dewormed, and 5 were not. Unfortunately, in most cases in this study, worm burden or ova counts were not made, so that the possible effect of treatment in decreasing the worm burden cannot be stated. Nevertheless, in all cases, the symptoms either were greatly alleviated or disappeared entirely. It must be stated, however, that most of the patients were aware of the diagnosis, and it is possible that the psychotherapeutic effect of a definite treatment for a definite disease contributed to the successful outcome.

infection. No attempt was made to compare the value of this method with that of other methods of detecting obscure cases of malaria, such as the complement-fixation test and examination of the blood smear following epinephrine injection. It is fair to state that subsequent improvement in the accuracy of routine laboratory blood examinations for the malarial plasmodia dampened our interest in sternal puncture. Examination of the literature on our return to this country, however, showed a similar enthusiasm for the method before¹¹⁻¹³ and since¹⁴⁻¹⁶ the onset of the war. Sternal puncture may be regarded as an expedient, safe and rapid method of investigating malaria that may be positive when repeated thick and thin blood smears fail to show the parasites. The method seems to deserve more extensive investigation in the future.

HOOKEWORM INFECTION

In the wake of the Papuan campaign there was, for a time, much preoccupation with the symptomless ovum passer and the attempt to render his stools free of hookworm ova. But the distinction between hookworm disease and hookworm infection and the over-all innocuousness of this infection in our troops were soon appreciated, and the condition dealt with more rationally. Some time later I analyzed a limited series of 70 patients at a general hospital in northeastern British New Guinea.

In the entire group the hemoglobin as determined by the Sahli method ranged from 11.8 to 14.8 gm, with a mean of 13.3 gm. In all but 4 cases the determinations exceeded 12.4 gm. The red-cell count ranged from 3,840,000 to 5,400,000, with a mean of 4,540,000. In only 1 case did the determination fall below 4,150,000. In view of the fact that, from a history of exposure, these patients had had the hookworm infection for from three to thirty months, it seems unlikely that, subsisting on the regular army diet, American troops developed any significant anemia from hookworm.

The symptomatology in this series could be divided into three general groups, the first of which comprised 43 patients with a multiplicity of symptoms, such as nervousness, tremor, apprehension, insomnia, nightmares, battle dreams, somnambulism, headache, dizziness, lethargy, depression, anxiety, temper outbursts, emotional instability and

This observation of lack of anemia is in agreement with the observations of Rhoads et al,¹⁷ who found that, in the presence of an adequate iron balance, anemia does not develop in patients with hookworm infection. In the present study, moreover, it appeared that the only soldiers with hookworm infection in whom treatment was helpful were the small group with purely dyspeptic symptoms. Furthermore, it is generally accepted that in the

absence of reinfection the hookworm eventually dies. The period of parasitism has been regarded as from a few months to several years. It is apparent, then, that from the immediate and long-run point of view, hookworm infection was largely innocuous in American soldiers. Hence the wise and expedient policy eventually formulated of treating ovum passers arbitrarily, of not following the effects of treatment unless the patient was to remain in the hospital for other reasons and of discharging him to duty possibly to have further stool examinations and treatment at a regimental dispensary. In the rare patient with a heavy infection, on the other hand, thorough treatment and adequate follow-up study were necessary.

MISCELLANEOUS DISEASES

Filariasis

A large number of soldiers were seen at the hospital in the summer of 1943 because of the probability of early filariasis. This group had been on Tongatabu, an island of the Samoan group, for exactly a year. Their symptoms were lymphadenitis,¹⁸ with fugitive dome-shaped swellings of the arms and legs, retrograde lymphangitis, varicocele, orchitis, epididymitis and recurrent funiculitis, the spermatic cord becoming enlarged, either spontaneously or after a deliberate exercise test,¹⁹ to several times its normal diameter. In all but 1 case in this entire group, repeated day and night smears failed to reveal the presence of microfilaria. Much more helpful diagnostic aids were the clinical course in soldiers who had been in endemic areas, an intelligently interpreted intradermal test and lymph-node biopsy with the finding of adult filarial worms or a characteristic tissue reaction. These men—familiar with the sight of native Tongans with advanced elephantiasis, envisaging a future behind a wheelbarrow full of scrotum and fearful of sterility in later life—were an extremely unhappy and apprehensive lot. Credit is due Major Paul Kunkel for the understanding and sympathetic way in which this group of soldiers was handled. The patients were told that in the absence of reinfection the likelihood of permanent changes was nil, this reassurance was vindicated by the subsequent course of events, as observed at special convalescent hospitals and elsewhere.^{20, 21}

Diphtheria

It was rather a surprise to learn that diphtheria is an important and widely prevalent tropical disease. Many cases of cutaneous and several of pharyngeal and nasal diphtheria were observed, as well as a few with residual peripheral-nerve palsies and one dying with, if not of, myocarditis. In a thoroughgoing investigation of this disease at Lae in British New Guinea, Cutts²² found that it was indeed the dermatologic wards that served as a constant reservoir of this infection. Cultures from the skin

of many patients with a wide variety of skin diseases showed virulent diphtheria bacilli. The lesions of skin diphtheria seen at this hospital were almost uniformly rather sharply defined, blackish to brownish-black, ulcerated areas with indurated bases,²³ yielding virulent diphtheria bacilli on culture, and located in traumatized areas about the heel or between the toes, where they were spindle shaped, and giving a suggestive if not characteristic appearance. Cutaneous diphtheria must constantly be thought of in the tropics or the diagnosis is apt to be missed.

During this overseas experience a large number of patients were seen with peripheral neuritis, some isolated, some multiple, some involving the scapulo-humeral group and producing the so-called "winged scapula" or involving the peroneal or other groups and some without and some with an elevation of the spinal-fluid protein in association with a normal or only slightly elevated cell count, producing the Guillain-Barré syndrome. In many of these cases early failure of the muscles of accommodation of the eye was suggested by the history or demonstrated by examination. Evidence accumulated during the course of the war became more and more conclusive that these neuritis were the residua of previous diphtheria, usually unrecognized.²⁴ If one is consulted by a veteran complaining of having developed "infantile paralysis" or some obscure neuritis during his tropical experience, it may be helpful to bear this point in mind.

Scrub Typhus Fever

This disease, with a mortality of from 2 to 30 per cent (average, 5 per cent), was far more serious than any other mentioned so far. It is caused by a rickettsia similar to those of epidemic and endemic typhus fever and of Rocky Mountain spotted fever. Its reservoir in New Guinea consists of certain field rats or voles or bandicoots, and its vector is a larval mite that clings, among other sites, to the lower portion of the stalk of the kunai grass, which is abundant on this island. The disease principally affected troops campaigning in uncleared areas. The acute illness is characterized by an eschar developing in a few days after the bite,¹ with marked regional and less marked generalized lymphadenopathy, chills, a high fever, a rash, the development of agglutinins against the Kingsbury strain of *Proteus bacillus*, cough, prostration, deafness, palsies and certain mental symptoms, such as headache, lethargy, delirium and coma. The disease generally runs a remittent course for two weeks, with evidence of pneumonitis and involvement of the cardiovascular system (tachycardia, hypotension, cardiac irregularities and gallop rhythm) supervening during the second week. All grades of severity were encountered, death generally occurring late in the second week. The most prominent post-mortem changes were a generalized

vasculitis and perivasculitis, with lymphocytic and plasma-cell exudation and with a predilection for the lungs, where an interstitial pneumonitis and hemorrhagic edema was produced, for the brain, where focal parenchymatous lesions referred to as "typhus nodules" eventually appeared, and for the heart, where the disease resulted in varying grades of diffuse interstitial or focal perivascular infiltrations of the same cellular types, as well as varying degrees of heart-muscle necrosis. Although there is no question that myocardial damage is present in the acute phase of the disease, the question whether these patients die in acute congestive heart failure is still debated.²⁵ Many of the survivors of this disease were debilitated for months and required prolonged periods of reconditioning before they could return to duty. Clinical²⁶ and pathological²⁵ studies following recovery showed no evidence of persistent myocardial damage and seem to indicate that much of the disability resides in the peripheral vascular system rather than in the heart.

Amebiasis

It should not be forgotten that many patients who have had amebic dysentery will continue to have diarrhea, presumably as a result of residual scarring of the bowel, even after the organism has been eliminated. In any patient with a history of amebic dysentery while in the service it is therefore essential to carry out a sigmoidoscopic examination and, if ulcers are present, to obtain swabbings or washings from the ulcers and to search for the organism. This may prevent the physician from initiating futile treatment. It is also well to remember that some of the drugs used in the treatment of amebiasis, such as chiniofon, are in themselves capable of inducing diarrhea.

* * *

To a civilian, the yellowed, underweight soldier returning from the tropics with a story of rigorous privation, starvation, extreme intolerable heat and disease conjures up an appalling picture of the "dank, steaming" malaria-ridden tropics. And yet the same civilian is amazed at the improvement in this soldier a month or two later, when he has excreted the quinacrine that was merely staining his tissues and when he has regained the weight lost as a normal physiologic reaction to the tropics. Is it possible, one might ask, that the soldier has failed to differentiate the unpleasant effects of field, combat or garrison conditions, with their attendant fatigue and boredom, from those due to the tropics per se? Many of the officers and enlisted men I questioned on this point admitted that life there in peacetime, with their families and with the conveniences and recreations and diet of the civilian, would not be unpleasant.

Interestingly enough, in spite of the high temperatures and humidities, no genuine cases of heat

stroke or heat exhaustion were observed during this service in New Guinea, Luzon and in semitropical Australia, presumably owing to an adequate process of acclimatization in the troops. Nor did the occasional elevations of temperature that had been expected on extremely hot days occur. In fact, many of my associates agreed that the days were much more comfortable than the so-called "dog days" of July or August in Washington or even in Boston.

SUMMARY

Medical experience in the Pacific in World War II has extended the knowledge of certain tropical diseases. Among other observations the following are noteworthy.

Quinacrine (Atabrine), at first regarded as a makeshift substitute for quinine, was found to be a more effective therapeutic and suppressive agent than the latter against malaria and eventually made that disease a relatively unimportant military problem.

So-called "chronic malaria" as it existed in American troops differed from the classic picture instead of anemia, malnutrition and asthenia, the troops presented various psychosomatic patterns largely without demonstrable organic disease.

Sternal puncture may reveal malarial plasmodia when repeated thick and thin blood smears fail to show the organism. In experienced hands, however, repeated thick and thin smears are satisfactory in the vast majority of cases.

Hookworm infection is to be distinguished from the hookworm disease. Parasitism is largely innocuous in American troops. Only parasitized troops with purely dyspeptic symptoms may expect relief from their symptoms after treatment.

Day and night blood smears are almost invariably negative in early filariasis. Lymph-node biopsy, the typical clinical course and skin tests, intelligently interpreted, are much more helpful in arriving at the diagnosis. Although fear of chronic invalidism was prominent in the minds of infected soldiers, evidence at hand indicates that permanent residua are unlikely.

Cutaneous diphtheria and, to a lesser extent, nasal and pharyngeal diphtheria are important tropical diseases. The dermatologic wards form a constant reservoir for the organism. Many cases of unrecognized diphtheria are followed by obscure neuritides, some with a Guillain-Barré type of spinal-fluid pattern.

Scrub typhus (tsutsugamushi) fever may produce severe fatal lesions of the heart, lungs or brain. There is neither clinical nor pathologic evidence of persistent heart disease following the infection.

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MEDICAL PROGRESS

DIGITALIS*

A. S. FREEDBERG, M.D.,† AND PAUL M. ZOLL, M.D.‡

BOSTON

IN RECENT years many reports have appeared on new purified digitalis preparations. Revisions have also been made in the *USP* unit of potency of digitalis, with changes in the method of assay as well as in the strength of the official preparation. Many cases of severe toxicity from digitalis have recently been reported¹⁻⁵ that indicate considerable confusion regarding the choice and dose of digitalis substances. It is the purpose of this paper to discuss the present status of whole-leaf digitalis and several purified digitalis bodies.

ASSAY

In the twelfth revision (1942) of the *United States Pharmacopoeia* the cat method of assay was employed for the first time. One cat unit is defined as the amount of digitalis per kilogram of cat weight that produces a lethal effect under certain defined conditions. One *USP XII* unit of digitalis represents the same potency as 0.1 gm of the *USP* digitalis reference standard powder, when assayed as directed. The digitalis leaves from which the reference powder was made, however, were of high potency, so that 1 *USP XII* unit is equivalent to 20 per cent more than 1 cat unit. It is particularly important for the physician to know the digitalis preparation he is using, since the clinical effect of

digitalis, standardized according to *USP XII*, is approximately 25 per cent weaker than *USP XI*, which in turn is approximately 50 per cent stronger than *USP X*.

The latest revision has led to more uniform preparations but has not solved the difficulties of assay. There are many variables inherent in the technic of assay by the cat method, such as the rate of injection,^{6,7} body temperature of the animal⁸ and depth and type of anesthesia. The increased toxicity of digitalis observed in cats with elevated body temperatures may be of clinical significance in explaining the deleterious effect of digitalis in patients with febrile illnesses. Further objections may be raised that the cat method of assay measures the lethal potency of digitalis and not specific therapeutic action.⁹⁻¹⁵ Bio-assays by other methods¹⁵⁻¹⁷ offer no advantages over the standardized cat procedure.

A chemical assay based on the presence of an active hydrogen atom in the unsaturated lactone group in digitalis has been developed.¹⁸ Further studies have shown, however, that the proposed chemical method does not measure total biologic activity¹⁹ and does not yield consistent results.²⁰

Human Method

Since the cat method of assay involves intravenous injection of digitalis substances, differences in absorption of the drugs from the gastrointestinal tract are not taken into account. Completely non-absorbable fractions may have significant potency according to the cat method of assay.²¹ Gold²²

*From the Medical Service and Medical Research Laboratories, Beth Israel Hospital and the Department of Medicine, Harvard Medical School. Aided by a grant from the Life Insurance Medical Research Fund.

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showed the error in translating potency of digitalis from cat units to clinical potency in man, by comparative assays in cats and human beings, a group of digitalis preparations with the same strength in cat units showed a tenfold range in potency in human subjects

The assay of digitalis preparations in human subjects has been developed by measuring the effect on the electrocardiogram. Bromer and Blumgart,²³ using the three standard leads, found that changes in the T wave of the electrocardiogram could be used as a quantitative index of the amount of digitalis effective within the body. In other studies,^{24, 25} which failed to demonstrate a quantitative correlation between the amount of the drug and the resultant electrocardiographic effects, only Lead 2 was recorded.^{24, 25} Although effects with digitalis were inconstant in the standard leads, Goldberger²⁶ noted the constant production of changes in the T waves and the ST segments in unipolar limb leads. More recently the quantitative effects of a digitalis substance on the electrocardiogram were measured by the analysis of the ventricular gradient.²⁷ This method is not yet suitable for human assay of digitalis.

Satisfactory assays in normal human subjects have been accomplished by Gold,^{28, 29} who produced qualitatively similar effects on the T wave and the ST segment with known and unknown preparations of digitalis. After control tracings (Leads 1 and 2) a dose of digitalis was given and the electrocardiogram repeated in twenty-four hours. In four experiments on the same subject, the electrocardiographic changes induced by doses of 100 per cent, 122 per cent and 149 per cent of a standard preparation of digitalis were compared with those following the digitalis substances to be assayed. The unknown preparations of digitalis were thereby assayed in human beings with an error of 25 per cent. Geiger et al.,³⁰ on the other hand, concluded that progressive digitalization produced electrocardiographic changes that were too small and inconstant to yield any quantitative correlation. A review of their actual data reveals, however, that in 3 of 10 normal subjects progressive digitalization caused increasing changes in the T waves. It was through the use of a few selected subjects like these that Gold was able to assay digitalis in human beings.

It is clear that such an assay is desirable because of the closer parallelism with clinical experience. Although the method proposed by Gold is the best available at present, its results have not yet been confirmed, it requires time, and relatively few subjects are suitable for assay. Furthermore, since the estimation of the electrocardiographic effect of digitalis depends on the judgment of the electrocardiographer regarding when equivalent changes in the T wave are produced, other causes of T-wave changes must be excluded. These include spontaneous variations and those induced by changes

in heart rate, as well as by food, drink, exercise, excitement, infections and fever, position and hyperventilation.³¹⁻³⁶

CARDIODYNAMIC EFFECTS

Since the assay of digitalis by the cat method is still imperfect and does not exactly reflect the clinical potency of the drug, the physician's skill is of paramount importance in the therapeutic use of digitalis. The rational use of digitalis demands understanding of its effects on the cardiovascular dynamics in congestive heart failure in human subjects.

It is almost universally agreed that administration of whole-leaf digitalis and purified glycosides in patients with congestive heart failure results in an increased cardiac output or a decrease in arteriovenous oxygen difference,³⁷⁻⁴⁹ lowered venous pressure^{41, 40, 43, 46, 47, 50-54} a faster circulation time^{41, 40, 47, 53, 54} and a diminished blood volume.^{55, 56} The fall in venous pressure may precede diuresis and slowing of the pulse rate.^{43, 51, 52, 54} Recently, Stewart et al.¹⁴ reported an increase in peripheral circulation as a whole after digitalization. The increase in cardiac output is obtained without a proportionate increase in cardiac work or oxygen consumption. The failure of cardiac output to return completely to normal after digitalis⁵¹ confirms the clinical evidence that most patients with congestive failure require additional therapy, such as limitation of activity, salt restriction and diuretics.

After digitalization the vital capacity is increased,^{45, 47} the respiratory minute volume is reduced^{38, 47, 57} and the alveolar carbon dioxide content is increased.⁴⁴ The basal metabolic rate falls.^{44, 44} Digitalization results in a decreased oxygen debt after exercise.⁵⁸

In patients with auricular fibrillation and a rapid ventricular rate digitalis induces significant slowing of the pulse rate. This effect has a twofold origin: vagal stimulation by therapeutic^{59, 60} or subtherapeutic^{61, 62} doses, which may be obliterated by atropine or exercise, and a direct action on the nodal tissues and myocardium, which cannot be obliterated thereby.

Considerable controversy exists concerning the exact mechanisms of the action of digitalis. According to some observers the therapeutic effect of digitalis is extracardiac in origin. Dock and Tainter^{63, 64} proposed another mechanism of action of digitalis — hepatic-vein constriction, with consequent reduction in venous return and in right auricular venous pressure, an effect comparable to venesection. Among other objections to this hypothesis is evidence that this mechanism does not obtain in human subjects.^{65, 66} The effects on vagal activity and the conducting tissues of the heart mentioned above do not account entirely for the beneficial response, which may occur without or before a change in rate. A large body of physiologic⁶⁷⁻⁶⁹ and electrocardiographic^{27, 70} data indicates a direct action of digi-

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0.5 mg for immediate digitalization^{30 51, 101, 109-112}, 0.1 mg may be administered every half hour to hour thereafter until full digitalization is accomplished. The short duration of action raises the problem of subsequent maintenance of digitalization. For this purpose, it has been recommended that, together with 0.5 mg of ouabain intravenously, whole-leaf digitalis be given orally — $\frac{1}{4}$ cat units to patients weighing less than 125 pounds, 6 to patients weighing 125 to 175 pounds, and 8 to patients weighing more than 175 pounds^{53, 109, 110}. At the end of twenty-four hours the patient may be placed on a daily maintenance dose of whole-leaf digitalis.

The only advantage possessed by the strophanthins over other purified glycosides is the rapid onset of action. Many considerations, however, make them unacceptable to the physician. Their stability in solution has been questioned¹⁰³. They are irritating when deposited extravascularly. Finally, maintenance of digitalization is difficult as a result of the short duration of action. Combinations with whole-leaf digitalis or other slowly acting drugs are difficult and unsatisfactory for routine use in that they often lead to toxicity or lack of adequate digitalization. In the relatively few emergencies in the treatment of congestive heart failure or paroxysmal arrhythmias, therefore, the physician uses to better advantage one of the other more stable, less irritating, purified glycosides with rapid and prolonged action.

LANATOSIDE C

Lanatoside C (digilanid C or Cedilanid) is the only one of the three lanatosides occurring in *Digitalis lanata* that is not present in *Dig. purpurea*. Many studies stimulated by the work of Moe and Visscher^{9 10} have been made comparing the potency, absorption from the gastrointestinal tract, speed of action and elimination, type of cardiac effect, therapeutic to toxic ratio, toxic effect and clinical effectiveness of lanatoside C with those of other preparations.

Absorption and Potency

Although the absorption of lanatoside C in animals¹¹³ is much faster and more complete than that of whole-leaf digitalis, studies in human subjects have yielded conflicting results¹¹⁴⁻¹¹⁸. The intravenous digitalizing dose in man of lanatoside C is agreed to be 6 cat units (16 mg), somewhat more than the oral and intravenous digitalizing dose of 3 cat units (12 mg) for digitoxin^{22 55, 116}. The single oral digitalizing dose for lanatoside C varied from 5 to 10 mg^{22 114 117}. The threefold to sixfold increase in oral over intravenous dose is due presumably to poor and variable absorption of the drug. It must be concluded that the absorption of lanatoside C is much less complete and more variable than that of digitoxin.

Time of Action

Accurate information is available regarding the relative speed and duration of action of lanatoside C. Following intravenous injection, the earliest effects were noted in ten to thirty minutes. This onset of action was measured by the fall in venous pressure,^{40 51 52 65, 69} slowing of ventricular rate,^{51 52 70} increased cardiac output,^{40 65, 69} diminution in diastolic heart volume or oxygen consumption,^{40, 65 69 113} and electrocardiographic changes.^{24 70} The effect is maximal in approximately two hours,⁷⁰ persists sixteen²⁴ to thirty-six hours⁷⁰ and disappears in three to six days.⁷⁰ In comparison with that of other glycosides, the onset of action of lanatoside C is slower than that of ouabain, similar to that of digoxin and considerably faster than that of digitoxin, the duration of effect is longer than that of ouabain and digoxin but considerably shorter than that of digitoxin.

Toxicity

No differences were found in the production of myocardial cellular damage¹¹⁹⁻¹²¹ and associated electrocardiographic changes^{122 123} by toxic doses of various glycosides, including lanatoside C. Kyser et al.¹²¹ related the probable mechanism to vagal stimulation and coronary constriction, since the lesions could be prevented by atropine or purines given at the same time as the digitalis drugs.

The prolonged intravenous administration of lanatoside C to dogs in small doses for over a year produced no harmful effect on the myocardium.¹²⁰ As with other glycosides, it does not reduce coronary blood flow at therapeutic or subtoxic levels.^{124 125}

In its ratio of minimal therapeutic to toxic dose, lanatoside C ranked next to ouabain and far above lanatosides A and B.^{9 10} Cattell and Gold,¹⁵ however, were able to demonstrate no difference in the ratio of therapeutic to toxic dose of a large number of cardiac glycosides, including lanatoside C. Nevertheless, many effects that contribute to the total toxic action of digitalis bodies cannot be observed in the experimental method employed.

Clinical Use

For intravenous digitalization 1.2 to 1.6 mg may be followed by subsequent administration of 0.4 mg at intervals of four to eight hours until the full digitalizing effect is noted. In this way, complete digitalization is rapidly reached and danger of toxicity reduced in spite of individual variations in susceptibility to the drug. Although 7.5 to 10.0 mg in two or three days is recommended in most studies for oral digitalization with lanatoside C, it has already been noted that there is a wide range in the required dosage. The broad range in the daily maintenance dose, from 0.5 to 3.0 mg, indicates the difficulty in maintenance of digitalization. This may be due to the rapid elimination and poor absorption of lanatoside C.

talism on heart muscle In this connection, Guttman⁷¹ has demonstrated the chemical union between digitoxin and striated muscle, such a combination with heart muscle has not yet been reported

WHOLE-LEAF DIGITALIS

Indications

In the light of the cardiodynamic effects of digitalis, it may be stated that the primary indication for the clinical use of digitalis is congestive heart failure Sufficient data are available to indicate the beneficial action of digitalis in congestive failure irrespective of the etiology of the disease or the type of cardiac rhythm^{4, 72-80} Additional indications include auricular flutter, persistent auricular fibrillation and heart disease associated with hypertension or valvular disease to prevent cardiac hypertrophy and congestive failure⁸¹⁻⁸³

Digitalis substances have been used successfully in the treatment and prevention of episodes of paroxysmal auricular tachycardia and paroxysmal auricular fibrillation^{80, 84-87} Although it has been assumed that the beneficial action in auricular arrhythmias is related to vagal stimulation, the mechanism of the action has not been established⁸⁸ The changes in cardiovascular dynamics that occur with constrictive pericarditis in the absence of auricular fibrillation, thyrotoxicosis, infection, shock and anemia are not indications for the use of digitalis

Contraindications

It should be stressed that there are no absolute contraindications to the use of digitalis in the presence of congestive heart failure In the absence of congestive failure contraindications include multiple ventricular extrasystoles and ventricular tachycardia, angina pectoris^{89, 90} or myocardial infarction,^{89, 91} recent or old, hypersensitivity of the carotid sinus,⁹² Stokes-Adams syndrome and partial heart block⁹³ Blumgart and Altschule,⁹⁴ however, showed that the administration of therapeutic amounts of whole-leaf digitalis to patients with partial heart block was not followed by an increase in the block

The effect of digitalis on intravascular clotting has recently been the subject of considerable investigation It has not yet been established that digitalis significantly alters the blood coagulation time⁹⁵⁻¹⁰⁰ It has been suggested that digitalis is a factor in the formation of fatal emboli by its thromboplastic effect or by the mobilization of endocardial thrombi^{91, 101, 102} The clinical data presented are not decisive

Clinical Use

Many schedules have been devised for the administration of digitalis^{80, 103-105} It must be remembered that routine administration strictly according to a preconceived plan is not advisable because of

variations in the drug and in the patient In most cases of congestive heart failure in which the drug has not been previously administered, digitalization may be accomplished by giving 0.3 gm of digitalis purpurea (*USP XII*) three times the first day and 0.1 gm three times daily thereafter until the optimal therapeutic effect or symptoms of minor toxicity appear Such a scheme avoids excessive delay in therapeutic result and also minimizes the risk of undesirable toxic manifestations In patients with auricular fibrillation and a rapid ventricular rate, slowing of the ventricular rate approximately to 70 is a satisfactory end point In patients with normal rhythm or with auricular fibrillation and slow ventricular rate, evidence of satisfactory digitalization consists of marked clinical improvement or the appearance of early toxic manifestations, such as anorexia and extrasystoles When a clear end point is reached, the drug may be discontinued for a day, if necessary, and a daily maintenance dose of 0.1 to 0.2 gm administered

A reliable preparation of whole-leaf digitalis should be used with which the physician is familiar, changing from one preparation to another is undesirable In the few cases in which whole-leaf digitalis is not tolerated or more rapid digitalization is needed a purified glycoside is preferable, either in a single oral dose or intravenously Recently, many purified preparations of digitalis bodies have been offered to the physician These are crystalline, do not require biologic assay and can be prescribed in terms of weight of the drug

STROPHANTHINS

Ouabain is obtained in pure crystalline form from *Acocanthera ouabain* and *Strophanthus gratus* From *Strophanthus kombé* is obtained K-strophanthin, an amorphous mixture of glycosides K-strophanthin-alpha (Cymarín), K-strophanthin-beta and K-strophanthoside are pure crystalline glycosides that have been isolated from this mixture The absorption of all these substances from the gastrointestinal tract is so irregular and poor that they are not suitable for oral use^{106, 107} Recently, Gold et al¹⁰⁸ studied a series of synthetic esters of the aglycone strophanthidin, one of which — the benzoate ester — was somewhat effective orally

Although the strophanthins induce the same qualitative physiologic effects after intravenous injection as digitalis, quantitative differences exist They are the most rapidly acting glycosides, inducing a decrease in ventricular rate and venous pressure in the first three or four minutes after administration,⁶¹ with a maximum effect in thirty⁶² to one hundred and twenty minutes⁶³ and a total duration of effect from twenty-four to seventy-two hours^{109, 110}

Clinical Use

It has been recommended that K-strophanthin or ouabain be given intravenously in doses of 0.3 to

The potency of 1 mg of digitoxin is approximately equal to 1000 mg of *USP XIII* digitalis reference powder. Thus, 125 mg of digitoxin induces the same degree of reduction of ventricular rate as 125 gm, or 163 cat units, of whole-leaf digitalis. The cumulative action of digitoxin is similar to that of whole-leaf digitalis, in patients with auricular fibrillation, the administration of small daily doses — 0.2 mg — resulted in a gradual decline of ventricular rate to normal levels in about three weeks.^{124 128} Maintenance of this dosage during a subsequent prolonged period induced no further change of rate. It may therefore be concluded that the excretion of digitoxin, like that of whole-leaf digitalis, is a function of the amount available within the body rather than the amount administered. Gold et al.¹²⁸ found no significant difference in the ratio between the toxic and therapeutic dose for digitoxin as compared to digitalis.

Toxicity

The toxic actions of digitoxin were first observed by Koppe,¹²⁹ who took 3.5 mg in five days, suffering severe toxic symptoms, nausea and vomiting, a slowing of the pulse rate from 80 to 40 and a bigeminal rhythm that became grossly irregular. Gold^{67 127} noted that a single oral digitalizing dose of digitoxin of 1.26 mg, or 3 cat units, induced nausea within two hours in only 2 per cent of a large series of patients. This was presumably due to the local gastric emetic action of digitoxin. An equivalent dose of whole-leaf digitalis produced early nausea in 20 per cent of the same group. With a single dose of 2 mg of digitoxin, 32 per cent of the patients developed minor toxic symptoms, and 20 per cent vomited. There seems to be ample evidence that digitoxin induces the same incidence of late or central toxicity as whole-leaf digitalis.^{140 141} Toxic doses of digitoxin, as with other glycosides, administered to animals are associated with the development of myocardial lesions,^{119 121} changes in the ST and T waves^{122 123} and a reduction in coronary blood flow.¹²⁵

Clinical Use

Stroud and VanderVeer¹²⁰ observed that the digitalizing dose of digitoxin was 1.3 to 2.2 mg when given orally over a period of three to six days. The maintenance dose was 0.1 mg daily. In many hundreds of patients with auricular fibrillation and a rapid ventricular rate Gold et al.^{124 128} found that a single oral or intravenous dose of 1.2 mg carried the process of digitalization fairly far.¹²⁴ They recommended subsequent daily doses of 0.2 mg to complete and maintain full digitalization. It must be remembered that full digitalization cannot be achieved promptly by this routine in all cases.^{59 125 141} In undigitalized patients, a single dose of 1.2 mg may be given by oral or intravenous route. The subsequent administration of digitoxin to

achieve full digitalization depends for its end point on whether the patient has auricular fibrillation with a rapid ventricular rate, auricular fibrillation with a slow ventricular rate or normal rhythm. In the presence of auricular fibrillation with a rapid ventricular rate, 0.2 to 0.4 mg should be administered at intervals of six to eight hours until the ventricular rate reaches approximately 70, it is not necessary to carry such patients to the point of minor toxicity. To complete full digitalization in patients with auricular fibrillation and a slow ventricular rate or with normal rhythm, additional digitoxin, in a dose of 0.2 to 0.4 mg, must be administered at intervals of six to eight hours until the earliest toxic symptoms are produced. It must be kept in mind that the desired clinical response may occur as a result of partial digitalization. In our experience, the subsequent maintenance dose has varied from 0.1 to 0.4 mg daily. In addition, despite the stated cumulative action of digitoxin, it has been necessary to redigitalize some patients with congestive failure at intervals of four to six months, even though they have been on large, apparently adequate, maintenance doses. When patients with auricular fibrillation become ambulatory close observation of the effect of exercise on the ventricular rate is necessary.⁵⁹⁻⁶¹ A sufficiently large maintenance dose should be administered so that exercise does not produce an excessive rise in ventricular rate.

In summary, the advantages of digitoxin are that it is a pure chemical that is stable and does not require bio-assay and that it is completely absorbed from the gastrointestinal tract, so that the oral and intravenous doses are the same and interchangeable. Furthermore, the small amount of digitoxin necessary for digitalization permits administration of a large fraction in a single dose, with only a small incidence of local gastrointestinal irritation. The rapid onset of action makes for quick digitalization by the oral route so that intravenous administration is rarely necessary. The prolonged duration of action, like that of whole-leaf digitalis, makes for easy maintenance. It is thus the drug of choice when a purified preparation is desired. Since there is some evidence that various preparations of digitoxin differ in potency, it is advisable for the physician, as with whole-leaf digitalis, to use a single preparation with whose action and potency he is familiar. The cost of digitoxin is at present considerably more than that of whole-leaf digitalis.

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Particular stress has been placed on the value of digitalis, particularly intravenous lanatoside C, for its rapid action in arrhythmias, such as paroxysmal auricular tachycardia, auricular flutter and auricular fibrillation, and even in chronic auricular flutter and fibrillation^{24, 80, 85, 87} Full digitalization was accomplished at the onset of the paroxysm and maintained by the daily use of 0.5 to 1.0 mg. over long periods. Although this schedule reduced the incidence of paroxysms, there is no evidence that lanatoside C accomplishes more than other digitalis preparations in the treatment of auricular disorders.

In summary, lanatoside C is a potent glycoside with all the actions of digitalis preparations. The advantages claimed, such as a greater margin of safety, greater cardiac efficiency and lack of reduction of coronary blood flow, are not yet proved in clinical practice. It is rapidly although poorly absorbed from the gastrointestinal tract. The relatively rapid excretion of lanatoside C, although perhaps a factor of safety in reducing the incidence and duration of toxic manifestations, is also a disadvantage, since maintenance of digitalization is difficult. The rapidity of effect on intravenous administration makes lanatoside C preferable to digitoxin in the relatively few acute emergencies in which the time differential may be important.

DIGOXIN

Digoxin, a purified glycoside isolated from lanatoside C by hydrolysis, is apparently the active cardiac principle in lanatoside C. Its physiologic effects on the heart and its toxic manifestations are similar qualitatively to those of the other digitalis bodies^{25, 43, 51, 52, 70, 126, 127}. Quantitative differences in the rate and extent of absorption from the gastrointestinal tract, as well as in the rate of elimination, differentiate digoxin from the others in clinical application.

Time of Action

Digoxin is similar to lanatoside C in its speed and duration of action, its effects become apparent in three to thirty minutes, are maximal in approximately one and a half to five hours and regress as early as eight to ten hours, being largely gone in twenty-four to thirty-six hours and completely absent in two to six days. These actions are appreciably more rapid than those of digitoxin. Batterman and DeGraff¹²⁸ clearly demonstrated the relatively rapid rate of elimination of digoxin. They digitalized 38 patients to the point of minor toxicity by giving 0.5 to 1.0 mg. of digoxin every six hours. After varying intervals, they repeated the administration with the same schedule to the same level of toxicity. The fraction of the initial dose necessary to reproduce the same level of toxicity after intervals of twenty-four, forty-eight and seventy-two hours was 49, 84 and 87 per cent respectively. These percentages indicate the amounts of the

drug lost in the intervals of time. The rapid elimination of the drug was further demonstrated in that, when an adequate single daily maintenance dose was given in divided portions, it became obviously insufficient, with resultant reappearance of congestive failure. This study is particularly cogent since a clear-cut, readily reproducible end point—namely, minor toxicity—was used, so that the same level of digitalization was clearly obtained even under conditions of clinical study. The usual objections to so many clinical investigations were avoided in that undefined levels of “full digitalization,” “desired cardiac effects” and “improvement in congestive failure” were not used.

Clinical Use

Many studies have clarified the clinical effectiveness of digoxin^{54, 78, 80, 104, 125, 127, 129, 130}. The average therapeutic and toxic doses on rapid oral administration were 3.75 and 6.0 mg. respectively, 1.0 to 2.0 mg. may be given initially, followed by 0.5 mg. every six hours until the desired effects are produced¹⁰⁴. For intravenous digitalization 1.0 mg. may be injected, followed by 0.5 mg. every six hours as necessary. The oral maintenance dose varied from 0.25 to 1.25 mg. daily. In some cases as much as 1.0 mg. three times daily was necessary for maintenance of digitalization¹⁰⁴.

In summary, digoxin is a potent substance that is valuable for rapid digitalization, with no particular advantage over lanatoside C. Its relative insolubility and irritating character make intravenous administration difficult. The difficulty of maintaining full digitalization over the long periods necessary in chronic congestive heart failure is a serious disadvantage.

DIGITOXIN

Digitoxin, or *digitaline crystallisée*, was isolated by Nativelle^{131, 132} in 1866 and was proved to be a potent cardiac drug by Vulpian.¹³¹ In 1875 Schmiedeberg¹³³ isolated a crystalline substance from digitalis leaves, which he named digitoxin, and stated that it formed the bulk of *digitaline crystallisée*. Although some data^{106, 134, 135} indicate that preparations of *digitaline crystallisée* and digitoxin differ in potency, the *United States Pharmacopoeia* treats them as if they were the same.

Pharmacology

Digitoxin is completely absorbed from the gastrointestinal tract in animals and human beings. Thus, the intravenous and oral doses are the same¹³⁵. If the oral absorption of digitoxin is judged by the decline in ventricular rate, it is complete in four to ten hours^{136, 137}. On intravenous injection the initial effects were noted in twenty-five minutes to two hours, with maximal effects in two to nine hours. Regression of effect began in two or three days, the total duration of action lasting approximately two weeks^{51, 67, 70, 134}.

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dilated, is displaced anteriorly, suggesting a retroperitoneal origin for the mass. The barium-enema study is rather unsatisfactory, probably because the patient was unable to hold the barium. The column ends in the descending colon, and so far as I can make out, there is no evidence of intrinsic disease, although there is marked displacement, as described in the record.

DR TAYLOR: This is a long history, and yet it includes few positive findings. The background of India is canceled out by the facts that no tropical

nauseated and vomited. Otherwise, the only findings were the large hard, partly fixed mass in the pelvis and the elevation of the white-cell count to 18,300.

What caused the pelvic mass? The elevated white-cell count at once makes us wonder whether an inflammatory mass was involved. If this patient had been older and had presented x-ray evidence of a diverticulum, one would wonder if the mass had arisen from diverticulitis of the colon, which sometimes causes large masses. The surprisingly



FIGURE 1

diseases are mentioned and that the patient had always been well while there. The examination by the flight surgeon before departure from India, with the finding of no abnormalities, should probably not be seriously considered. I believe that the flight surgeons may have overlooked masses the size of a grapefruit or watermelon. The patient did have a mass when he arrived in this country, however, and was astute enough to recognize it himself. The only preceding episode was the brief attack of knife-like pain followed by the passage of flatus on the trip home. In the hospital, the patient felt

negative history of any relation to episodes of inflammation in the past, however, makes one doubt that. Similarly, an appendiceal abscess frequently gives rise to a large mass, but again there is nothing in the background except for one brief episode of pain. If we had to go seriously into the background of tropical diseases I should not know what to call a mass originating in a patient who had been in India. If he had been in South America, one would wonder about echinococcal disease in some form. Certainly against inflammatory disease is the absence of anything suggesting an inflammatory

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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CASE 32521

PRESENTATION OF CASE

A forty-five-year-old schoolmaster entered the hospital because of an abdominal mass associated with crampy abdominal pain.

Thirty days before admission the patient had had a short attack of knifelike suprapubic pain that was accompanied by the passage of considerable gas by rectum. At that time he was en route from India to the United States. He had served in India for three years with the United States Army Air Force during which time he had felt entirely well and had had no tropical diseases. Examination had been carried out by a flight surgeon shortly before departure, and no abnormalities had been noted. On arrival in the United States the patient noticed the appearance of a lower abdominal mass. This was called to the attention of a physician, who found a nontender symmetrical mass in the suprapubic area about the size of a large grapefruit, this extended to the umbilicus. The patient was referred to a genitourinary consultant, who catheterized the bladder and found no residual urine. The mass did not change on catheterization. The patient was then referred to the hospital. On entry he stated that the day before admission he had felt nauseated and had vomited twice, this was the only episode of nausea and vomiting that had occurred. The bowel movements had been normal except that an unusual amount of gas had been passed by rectum, there had been no mucus or blood. There had been no urinary symptoms or weight loss.

The past history was irrelevant except for pneumonia in childhood and a tonsillectomy as a young man. The family history revealed that the patient's mother had died of diabetes, and his grandmother, of cancer.

Physical examination disclosed a well nourished patient in no acute distress. The lower abdomen was slightly protuberant. A large, hard, nodular tumor extended upward in the midline from the pelvis to the area of the umbilicus. It was quite fixed in position and seemed to be adherent to the

abdominal wall. Some portions of the mass were slightly tender. Rectal examination was negative. The heart and lungs were normal.

The temperature was 98.6°F, the pulse 86, and the respirations 20. The blood pressure was 138 systolic, 80 diastolic.

Examination of the blood showed a red-cell count of 4,280,000, with a hemoglobin of 13 gm per 100 cc, and a white-cell count of 18,300, with 82 per cent mature neutrophils, 7 per cent young neutrophils and 11 per cent lymphocytes. The urine was normal except for a + test for albumin in one specimen. The nonprotein nitrogen was 27 mg and the serum protein 6.9 gm per 100 cc. The chloride was 94 milliequiv per liter. A stool specimen was brown and gave a negative guaiac reaction. Routine x-ray films of the chest were negative.

Roentgenographically, the kidneys appeared normal in size and position, and intravenous dye was promptly excreted by both kidneys. There was some distention of the right ureter and to a lesser extent of the left midureter, and there was delay in passage of the dye at the level of the sacrum (Fig. 1). The bladder shadow was compressed superiorly by what appeared to be an ill defined midline mass filling the basin of the pelvis. In the lateral view the right ureter appeared displaced anteriorly. There was a small calcified lymph node in the midabdomen. Visualized bones showed no evidence of intrinsic disease. There was spina bifida of the fifth lumbar vertebra without displacement. An attempted examination of the colon showed the sigmoid loop to be displaced downward and compressed toward the left, and barium could not be found beyond that point. It was stated that the films showed no definite evidence of intrinsic disease of the colon.

On the fourth hospital day proctoscopy revealed a sharp posterior angulation 16 cm from the anus that stopped the progress of the instrument. The mucosa was normal, and there was no evidence of ulceration, bleeding or intrinsic tumor. Cystoscopy was attempted, the compression of the bladder from without prevented sufficient distention to enable its mucosa to be visualized.

Except for slight daily elevations of temperature to 99.5°F, there was no change in the patient's condition. On the sixth hospital day an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. GRANTLEY W. TAYLOR: May we see the x-ray films?

DR. JAMES R. LINGLEY: The margins of the mass are not well defined on the film, but the presence of a mass may be inferred from the evidence of marked pressure on the superior margin of the bladder, with flattening of the bladder shadow, and from the evidence of obstruction of both ureters. In the lateral view one ureter, in addition to being

Taylor's, nor did we take into consideration so many points. We differed when we came to the final analysis and swung in favor of tumor instead of appendiceal abscess, thinking that it probably was a retroperitoneal sarcoma. The only x-ray examination that we did not make was a small-bowel series. At that time we could not visualize a primary lesion of the small bowel that would cause so much difficulty without intestinal obstruction. In retrospect, we should have considered the special tumor of the small bowel that is characterized by distended bowel and not by obstruction.

When we opened the abdomen the first thing visible was massive edema anterior to the peritoneum. Within the peritoneal cavity there was a greatly dilated, perforated loop of ileum. There was a large abscess walled off by the sigmoid. There was a sharp demarcation between normal small bowel and the tumor area, the latter was about 60 cm long. There were also huge lymph nodes in the mesentery, some being as large as 3 cm in diameter. When we saw the gross specimen we were fairly sure of the diagnosis of lymphoma. While the pathologist was examining the tumor, we went ahead with resection of the small bowel and anastomosis.

DR MALLORY: Frozen section of the tumor showed obvious neoplastic disease, which we thought was lymphomatous. That was confirmed by the sections of fixed tissue. Both the bowel wall and the mesentery were diffusely invaded by tumor composed almost entirely of immature lymphocytes, and we classified the lesion as lymphoblastic lymphoma.

Were you able to verify whether or not the retroperitoneal tissues were involved, Dr Welch?

DR WELCH: We could not tell because of the tremendous amount of edema.

DR MALLORY: It had extended so far back into the mesentery that I think it probable that they were.

DR WALTER BAUER: Was this a lymphoblastic type of lymphoma arising in the small intestine?

DR MALLORY: I cannot say whether it arose in the small intestine and invaded the mesentery secondarily, or whether it was in the mesenteric lymph nodes and involved the small bowel.

DR BAUER: And there was never more interference of bowel habit than that mentioned in the record?

DR MALLORY: In lymphoblastoma I have seen 12 to 50 cm of small bowel thickened to the appearance and almost the stiffness of a rubber hose, with no intestinal symptoms.

DR BAUER: Is there a type of lymphoblastoma that is confined to the small intestine and may be cured by resection? If so, what type is it?

DR MALLORY: Any one of the types. We have seen isolated lymphomatous tumors with prolonged

cures after resection in the stomach, the small bowel and the large bowel.

DR BAUER: Have the cures lasted five to twenty years?

DR MALLORY: I am sure that I have seen cures as long as ten years. Beyond that I do not want to say.

DR BAUER: Is that equally true with any of the lymphomatous tumors, the reticulum-cell, the lymphocytic or the lymphoblastic type?

DR MALLORY: One probably has a better chance with a reticulum-cell sarcoma, but I have seen such cures with several types.

DR BENJAMIN CASTLEMAN: Several years ago Dr Gall* reported a series of such cases that had been observed here.

DR TAYLOR: I should like to ask Dr Welch if the mass was primarily inflammatory or whether it chiefly consisted of tumor.

DR WELCH: It was practically all an inflammatory mass.

*Gall E. A. and Mallory, T. B. Malignant lymphoma: clinicopathologic survey of 618 cases. *Am J Path* 18:381-429, 1942.

CASE 32522

PRESENTATION OF CASE

A sixty-two-year-old housewife entered the hospital because of persistent drainage from a cecostomy.

About five years before admission the patient first began having attacks of abdominal pain in the left lower quadrant. These lasted a day or two and were accompanied by a feeling of tenesmus and by loose stools. Between attacks there was no discomfort. The stools gradually became smaller in size but never contained blood and were never black. About fifteen weeks before admission, during an unusually severe attack of pain, the left side of the abdomen was found to be swollen. At that time an operation was performed. The only available details were that an incision had been made in the left lower quadrant, and that a cecostomy had been performed. After the operation the patient was too weak to do more than sit up in a chair for a part of each day. The cecostomy functioned well. Subsequently, a small amount of fecal matter and some mucus were passed by rectum, but never any blood. There had been a weight loss of 13 to 15 pounds in the two months preceding admission. Except for occasional pain on motion of the knees and elbows and slight exertional dyspnea, there were no complaints.

Physical examination showed a moderately obese woman. The abdomen was slightly distended. There was a well healed incision in the left lower quadrant. There was a functioning cecostomy whose mucosa was widely everted. Vaginal examination revealed a normal cervix and a uterus whose fundus was barely palpable in normal position.

process, except the elevation of the white-cell count and the slight rise of the temperature to 99.5°F in the hospital

So we move on to tumors. The only thing we can be grateful for in an otherwise confusing picture is that this patient was not a woman and that we do not have to consider the female genital tumors. It is bad enough as it is. The x-ray evidence regarding the location of the tumor is complicating in the sense that one ureter was pushed forward, suggesting a retroperitoneal origin for the mass. On the other hand, the sigmoid colon seemed to be knuckled backward when palpation was attempted, suggesting an intra-abdominal mass flexing the colon backward. It is hard to see how a retroperitoneal mass would do that to the colon.

From here on it becomes a matter of guessing what kinds of pelvic tumors occur in patients who are practically asymptomatic. We always fall back on the retroperitoneal fibrosarcoma as an explanation for many tumors, and that does not do much more than characterize the histology. We know little about the process, which is a rather frequent finding in a large hospital such as this, I suppose we have a number of them each year that are called retroperitoneal fibrosarcoma. As a rule, when such tumors achieve the size of the one in this case, there is evidence of vascular or lymphatic blockage, as well as a suggestion of associated edema of one extremity and evidence of stasis in the lymphatic or venous return. That is perhaps because the tumor not only causes pressure on the vessels but may actually invade them and propagate in them as a growing tumor thrombus.

A tumor that is frequently seen in this location is the chordoma — another tumor that we do not know a great deal about. As a rule, I believe that all such cases show some evidence of bone destruction because of their locus of origin. They are slow in their progress, and it seems likely that a chordoma that had achieved the size of the tumor in this case would have been observed for many years rather than a brief time. Dermoid cysts that originate in this part of the body are sometimes practically asymptomatic, they are usually symmetrical and smoothly outlined, and the nodular character of the tumor in this case argues against dermoid, unless secondary malignant degeneration had occurred.

Tumors of the lymphoblastic series are usually multiple, sometimes there is a large single tumor, which may appear as a retroperitoneal mass. The negative x-ray findings justify us in ruling out some of the other things that occur to one asked to define the cause of a pelvic tumor. Sometimes, ectopic kidneys, which are infected or otherwise, may become quite large, causing a great deal of trouble for the patient. Bone tumors and chondrosarcoma often reach enormous size and may be located in this region. The primary tumors of the bowel

rarely develop to this extent, and certainly without bowel symptoms they are practically unheard of. Consequently, this tumor must have occurred in tissues that are found in this general region, having no association with any specific organ, if neoplasm is to be regarded as accounting for this patient's symptoms.

Could neoplasm account for the elevation of the white-cell count and temperature? I think that in certain circumstances it could, but the white-cell count was rather high and the young neutrophils suggest that an active inflammatory process was going on somewhere. One neoplasm that I did not allude to, — and I swing back to the appendix again, — is a carcinoid, which may involve the appendix and may become a tumor of significant size, although I have never heard of any carcinoid nearly approaching this one in extent. If I must commit myself, I think that the diagnosis is more probably appendiceal abscess, with a mass around it, than a primary pelvic neoplasm. I base that statement partly on the rapid development, partly on the fact that there was not much in the way of pressure obstruction of the circulatory apparatus of the lower extremities and partly on the specific character of the tumor as described on palpation, since it was much higher in the pelvis than a great many of the tumors to which I have referred. They usually occupy the true pelvis, not the pelvic canal, and are palpable on rectal examination, whereas this tumor was well up and above that, although in the x-ray film it appears to descend fairly low.

A PHYSICIAN: Could the right ureter have been drawn forward rather than pushed out by the mass?

DR TAYLOR: I should think that it could.

DR ROLF LUFT*: In Sweden, years ago, a nurse in a hospital had a large tumor mass in the pelvis that was described as Symmer's disease and that originated in the retroperitoneal lymph nodes.

DR TRACY B MALLORY: Symmer's disease is usually called giant follicular lymphoma in this country.

CLINICAL DIAGNOSES

Sarcoma compressing rectosigmoid, bladder and ureters

Hydronephrosis

DR TAYLOR'S DIAGNOSIS

Appendiceal abscess

ANATOMICAL DIAGNOSIS

Lymphoblastic lymphoma of small bowel

PATHOLOGICAL DISCUSSION

DR CLAUDE E. WELCH: The differential diagnosis on the surgical service was not so thorough as Dr

*Of Stockholm, Sweden.

Taylor's, nor did we take into consideration so many points. We differed when we came to the final analysis and swung in favor of tumor instead of appendiceal abscess, thinking that it probably was a retroperitoneal sarcoma. The only x-ray examination that we did not make was a small-bowel series. At that time we could not visualize a primary lesion of the small bowel that would cause so much difficulty without intestinal obstruction. In retrospect, we should have considered the special tumor of the small bowel that is characterized by distended bowel and not by obstruction.

When we opened the abdomen the first thing visible was massive edema anterior to the peritoneum. Within the peritoneal cavity there was a greatly dilated, perforated loop of ileum. There was a large abscess walled off by the sigmoid. There was a sharp demarcation between normal small bowel and the tumor area, the latter was about 60 cm long. There were also huge lymph nodes in the mesentery, some being as large as 3 cm in diameter. When we saw the gross specimen we were fairly sure of the diagnosis of lymphoma. While the pathologist was examining the tumor, we went ahead with resection of the small bowel and anastomosis.

DR. MALLORY: Frozen section of the tumor showed obvious neoplastic disease, which we thought was lymphomatous. That was confirmed by the sections of fixed tissue. Both the bowel wall and the mesentery were diffusely invaded by tumor composed almost entirely of immature lymphocytes, and we classified the lesion as lymphoblastic lymphoma.

Were you able to verify whether or not the retroperitoneal tissues were involved, Dr. Welch?

DR. WELCH: We could not tell because of the tremendous amount of edema.

DR. MALLORY: It had extended so far back into the mesentery that I think it probable that they were.

DR. WALTER BAUER: Was this a lymphoblastic type of lymphoma arising in the small intestine?

DR. MALLORY: I cannot say whether it arose in the small intestine and invaded the mesentery secondarily, or whether it was in the mesenteric lymph nodes and involved the small bowel.

DR. BAUER: And there was never more interference of bowel habit than that mentioned in the record?

DR. MALLORY: In lymphoblastoma I have seen 12 to 50 cm of small bowel thickened to the appearance and almost the stiffness of a rubber hose, with no intestinal symptoms.

DR. BAUER: Is there a type of lymphoblastoma that is confined to the small intestine and may be cured by resection? If so, what type is it?

DR. MALLORY: Any one of the types. We have seen isolated lymphomatous tumors with prolonged

cures after resection in the stomach, the small bowel and the large bowel.

DR. BAUER: Have the cures lasted five to twenty years?

DR. MALLORY: I am sure that I have seen cures as long as ten years. Beyond that I do not want to say.

DR. BAUER: Is that equally true with any of the lymphomatous tumors, the reticulum-cell, the lymphocytic or the lymphoblastic type?

DR. MALLORY: One probably has a better chance with a reticulum-cell sarcoma, but I have seen such cures with several types.

DR. BENJAMIN CASTLEMAN: Several years ago Dr. Gall* reported a series of such cases that had been observed here.

DR. TAYLOR: I should like to ask Dr. Welch if the mass was primarily inflammatory or whether it chiefly consisted of tumor.

DR. WELCH: It was practically all an inflammatory mass.

*Gall, E. A., and Mallory, T. B. Malignant lymphoma: clinicopathologic survey of 618 cases. *Am J Pathol*, 18:381-429, 1942.

CASE 32522

PRESENTATION OF CASE

A sixty-two-year-old housewife entered the hospital because of persistent drainage from a cecostomy.

About five years before admission the patient first began having attacks of abdominal pain in the left lower quadrant. These lasted a day or two and were accompanied by a feeling of tenesmus and by loose stools. Between attacks there was no discomfort. The stools gradually became smaller in size but never contained blood and were never black. About fifteen weeks before admission, during an unusually severe attack of pain, the left side of the abdomen was found to be swollen. At that time an operation was performed. The only available details were that an incision had been made in the left lower quadrant, and that a cecostomy had been performed. After the operation the patient was too weak to do more than sit up in a chair for a part of each day. The cecostomy functioned well. Subsequently, a small amount of fecal matter and some mucus were passed by rectum, but never any blood. There had been a weight loss of 13 to 15 pounds in the two months preceding admission. Except for occasional pain on motion of the knees and elbows and slight exertional dyspnea, there were no complaints.

Physical examination showed a moderately obese woman. The abdomen was slightly distended. There was a well healed incision in the left lower quadrant. There was a functioning cecostomy whose mucosa was widely everted. Vaginal examination revealed a normal cervix and a uterus whose fundus was barely palpable in normal position.

There was induration high in the left vault. On rectal examination there appeared to be a mass fixed high to the lateral pelvic wall on the left that did not involve the rectal mucosa. Proctoscopy for a distance of 15 cm showed a normal mucosa. Further progress of the proctoscope was stopped by angulation of the bowel.

Examination of the blood revealed a hemoglobin of 12.4 gm per 100 cc and a white-cell count of 10,200, with 69 per cent neutrophils. The urine gave a + test for albumin, and rare granular casts, 2 red cells and 50 white cells per high-power field were found in the sediment. Barium filled the rectum and distal sigmoid readily. In the mid-sigmoid there was an area of constant narrowing, extending for a distance of about 8 cm (Fig 1), in one portion there appeared to be an absence of the mucosa in a small area, but the remainder of the mucosa looked normal. There was an indefinite



FIGURE 1 Plain Film of Abdomen following a Barium Enema

suggestion of a shelf defect distally and of rounded, filling defects in the lower portion of the lesion.

An operation was performed on the sixth hospital day.

DIFFERENTIAL DIAGNOSIS

DR. WALTER GARREY: It might be instructive to comment briefly about the history and physical findings before we look at the x-ray films. The patient was a sixty-two-year-old woman who for five years had had brief attacks of pain in the left

lower quadrant lasting a day or two, with a feeling of tenesmus and the passage of loose stools. This certainly suggests a recurring inflammatory process in the bowel. Then the patient gave evidence of a gradually increasing degree of chronic, low, large-bowel obstruction — she was definite that the stools had become smaller in size. She had never noticed any blood, although, of course, she may have overlooked it. She had a severe attack of pain and was operated on; apparently, the lesion found was such that the surgeon decided merely to relieve the large-bowel obstruction by doing a cecostomy but did not defunction the bowel with a colostomy. Four months later she was admitted to this hospital, where a mass was found high up in the left pelvis or low in the left lower abdomen. She had a slight degree of anemia and claimed to have lost a little weight. I suppose that the urine was a voided specimen, if so, the white-cell count means little.

May we see the x-ray films?

DR. JAMES R. LINGLEY: This area in the colon, just above the midsigmoid, shows a definite narrowing. No diverticula are visible, and on the inferior margin of the bowel there appear to be round defects. I cannot be too sure of the mucosa in that film, but I think that there is definite evidence of masses in the bowel wall.

DR. GARREY: But there is sufficient filling of the rest of the colon, so that if there had been diverticula farther up the colon they would have shown?

DR. LINGLEY: I think that they would have shown.

DR. GARREY: Is this an annular lesion?

DR. LINGLEY: No, I think that it involves chiefly the lower margin of the bowel and that there is intact mucosa above.

DR. GARREY: Is there a definite ulcer at this spot?

DR. LINGLEY: The fluoroscopist described an ulcer. I cannot be certain from the films.

DR. GARREY: This history could be explained by an inflammatory process because of the recurring attacks for a long time. Far and away the most frequent of all these is a diverticulitis of the sigmoid. The midsigmoid is the likeliest location for diverticulitis, and the chronic obstructing form of diverticulitis easily gives an 8-cm cylindrical obstructing lesion with a normal mucosal pattern, the obstruction being due to a woody-hard, inflammatory reaction in the walls of the bowel. The fact that no blood was noted fits perfectly well with diverticulitis. In the different series of cases of diverticulitis reported, blood has been found in from 6 to 30 per cent. One expects to find blood in cases of carcinoma — even if the patient has not noted it, it is usually found on chemical testing. We have no information whether such tests were done. In over 90 per cent of cases that have diverticulitis in the midsigmoid one or more diverticula are found elsewhere in the colon. None were found in this case, despite fairly good filling. The fact that the obstruction produced by this lesion did not subside

after a cecostomy is no contraindication to the diagnosis of chronic obstructing diverticulitis. In the first place, the bowel was not defunctioned, and many cases on record go for even twelve months with little relief in the inflammatory thickening of the bowel after cecostomy.

What other conditions should we consider? There was an unusual case, seen in this hospital a few years ago and discussed at one of these conferences by Dr McKittrick,¹ of endometriosis involving the sigmoid in a woman past the menopause, but the area of endometriosis and narrowing of the sigmoid was small. With this 8-cm obstruction, or nearly complete obstruction, intussusception of that area is certainly a possibility but a rare and most unusual eventuality.

Could this have been a tuberculous inflammatory lesion? I think that the size and the lack of a large ulcer, as well as the location in the left rather than in the right colon, are against that diagnosis.

Could this have been any form of benign tumor? Such tumors are extremely rare in the colon. Lipomas occur but certainly do not give an 8-cm-long cylindrical type of obstruction. I do not believe that this was a lipoma.

Could the obstruction have been due to something extrinsic to the colon and involving it secondarily? It is possible that cancer of the ovary invaded the sigmoid, but after such a long period, I should expect the patient to have had ascites or signs of dissemination rather than a localized process in the bowel itself.

Another possibility is that, over this long period, some premalignant lesion, such as an adenomatous polyp, was present and that eventually a slowly growing neoplasm developed and invaded the bowel, infiltrating upward in the mucosa, so that part of the mucosal pattern was visible and yet there was some ulceration. I think that that is a good possibility. We are not told whether any tests for blood were made on the stools.

DR TRACY B MALLORY: There is no record of any tests on the stools.

DR GARREY: Could this have been a diverticulitis of the chronic obstructing type, accounting for the history of recurring episodes, with the subsequent development of a carcinoma of the sigmoid, so that there was a double diagnosis? That is possible, and it is interesting that in a series of 40 cases recently reported by Dr Young,² 2 such examples of double lesions were not correctly diagnosed either by x-ray or other studies beforehand. In these exercises, however, it is safer to make one diagnosis than two. Since we are told that there were nodular filling defects in the bowel and an area in which there was

normal mucosa and still another area in which there was ulceration, I shall call this carcinoma, but I think that diverticulitis could perfectly well explain the entire picture.

DR ARTHUR W ALLEN: Dr Garrey has covered this situation exceedingly well. I should like to emphasize one of his last statements. I was afraid that he was not going to mention the diagnosis of carcinoma of the sigmoid, with coincident diverticulitis. That is a fairly frequent finding. Every series of reported cases of diverticulitis or diverticulosis of the sigmoid includes a certain number of such cases. There is a good deal of disagreement concerning the significance of bleeding in the differential diagnosis. Dr Harvey Stone is sure that bleeding can occur from diverticulitis alone. Dr Vernon David, on the other hand, states that with bleeding in a case of diverticulitis of the sigmoid one must assume that carcinoma is present. Both are right to a certain extent. It may interest Dr Garrey to know that the surgeon who first explored this patient and did the cecostomy made the diagnosis of carcinoma, in the acute stage such a diagnosis is frequent. It is difficult to tell by palpation or exploration whether the lesion is inflammatory or neoplastic. We thought that this woman had cancer, but we were wrong. It is only fair to say that we were influenced to some extent by the x-ray finding of the mucosal defects and so forth. It could well have been carcinoma on the basis of the history, in spite of the diverticulitis, as Dr Garrey has pointed out.

CLINICAL DIAGNOSIS

Carcinoma of sigmoid

DR GARREY'S DIAGNOSIS

Carcinoma of sigmoid, superimposed on diverticulitis

ANATOMICAL DIAGNOSIS

Diverticulitis of sigmoid

PATHOLOGICAL DISCUSSION

DR MALLORY: The resected specimen showed a localized area of diverticulitis, with a chronic inflammatory process in the bowel wall accounting for the contraction of the bowel lumen. There were numerous diverticula, all solidly plugged with fecaliths, which explains why the barium did not fill them. There was no evidence of neoplasm.

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HAPPY NEW YEAR

CHRISTMAS and New Year, as was suggested on this page last week, travel well together. They are as companionable as Damon and Pythias, as Troilus and Cressida, as ham and eggs, as inseparable in our minds as David and Goliath or as a pick and its shovel. They are more than that: they are almost, although not quite, identical images that have been carelessly imposed on each other. There they are, as like as two peas, but the edges are a little blurred.

They could well have been identical if our old time astronomers had been able to calculate a little more closely, for they both mark the turning of the season, only both are a little late — an almost human failing. It is the Christian Church that attached the religious significance to the pagan festival that is

now Christmas. The New Year, too, has its pious resolutions.

Perhaps it is just as well that Christmas and New Year are a week apart, from a practical point of view. Some heads would hardly be equal to eggnog in the morning and wassail in the afternoon. The present juxtaposition, moreover, without exact identification, like the blurred image, gives us what we really want in midwinter — not simply a holiday, too intense, but a holiday season.

The idea of the Happy New Year, as a greeting, is a good one. No one has really expected, during the last five thousand years or so since civilization began, that the impending year would really be a happy one, and it is surprising how often so many of us have been agreeably disappointed. There has always been someone on every street corner waiting for the world to fall apart, and as a rule most of these, too, have had to turn their grudging footsteps homeward.

Our prediction is that the coming year will bring a number of industrial and international crises, a certain amount of snow and rain and some fair weather and a good deal of hollering by all concerned. At its end we shall find ourselves in port with a few loose rivets, and continue making gloomy forecasts for 1948.

And so, with considerable assurance, we wish all our readers — a select group — our usual Happy New Year!

SYPHILIS AND PENICILLIN

MANY reports have been published indicating the response of syphilis to penicillin therapy. Physicians in general have been quick to adopt this new medicinal agent, and the laity has developed an enthusiasm about its use in syphilis and other diseases that may require some curbing. It is well, therefore, to review with care some of the problems arising in the course of penicillin therapy, such as is done elsewhere in this issue of the *Journal*. Problems arise in connection with the penicillin-resistant case and in matters of relapse, reinfection and reactions. Public-health aspects, including the question of the returning veteran and marriage, are topics of concern in connection with penicillin.

therapy These and other matters must be carefully considered, especially in the light of the gradually increased dosage of penicillin that is being recommended from time to time following careful studies of treated cases Some of these patients did not receive enough penicillin to cure their syphilis and have relapsed or will relapse

The matter of relapse is of special significance In the group of clinics sponsored by the National Research Council and the United States Public Health Service the cumulative percentage failure at the end of eleven months after treatment varied from 15 per cent with a dosage of 2,400,000 units of penicillin to 62 per cent with one of 600,000 units ¹ About 10 per cent of these failures were actually due to reinfection, but the rest were relapses Various treatment schedules were used in the different co-operating clinics, and in general it can be said that there were fewer failures when both arsenic and bismuth were used in combination with the penicillin.

Another complication has been added by the changing character of commercial penicillin ² Various fractions of penicillin have been found and designated G, X, F and K Penicillin K is relatively inefficacious, since it is rapidly destroyed in the body, this assumes significance because of the fact that certain commercial penicillins have recently shown an increasing content of penicillin K It is also not known as yet whether increasing purification of penicillin removes some of the substances that have great therapeutic activity

As a result of reviewing these cases in the various co-operating clinics it has been suggested that for seronegative primary syphilis the minimum dose of the at-present-available penicillin should be not less than 3,600,000 units, given intramuscularly in doses of 40,000 to 60,000 units at two-hour or three-hour intervals For seropositive and early secondary syphilis a dose of not less than 5,400,000 units is recommended If a relapse occurs, arsenic and bismuth should also be given when the course of penicillin is repeated Penicillin by mouth is not advocated Thus, the treatment of syphilis by penicillin has repeatedly been modified as further study of treated cases has progressed

Emphasis is placed on the fact that the present recommendations are only tentative and are subject to revision as the results of treatment are fur-

ther studied The eventual value of penicillin in syphilis is still uncertain, and its ultimate status will not be established for several years to come To be sure that syphilis has been successfully treated by any new procedure requires a long period of observation, measured in terms of years, not months Every physician thus has a particular responsibility for the careful follow-up, serologic and clinical, over a period of years of every penicillin-treated case of syphilis that he sees, whether the penicillin was received in civilian life or during military service

REFERENCES

- 1 Committee on Medical Research and United States Public Health Service Treatment of early syphilis with penicillin *J A M A* 131 265 271 1946
- 2 Committee on Medical Research United States Public Health Service and Food and Drug Administration Changing character of commercial penicillin with suggestions as to use of penicillin in syphilis. *J A M A* 131 271 275 1946

MASSACHUSETTS DEPARTMENT
OF PUBLIC HEALTH

GROUP DONATIONS TO THE MASSACHU-
SETTS BLOOD DONOR PROGRAM

Many social and fraternal organizations are obtaining the benefits of the services and protection offered by the Massachusetts Blood Donor Program by making group donations when the Mobile Unit visits their community By having at least 10 per cent of the total membership of the organization donate to the program, every member in the entire group becomes eligible to receive whole blood, plasma or fractions when needed

Details of the plan for group participation are simple Any organization desiring to donate in a body should communicate with its local Red Cross chapter, expressing a willingness to take part in the program Arrangements for the registration of and appointments for donors can be worked out jointly by group directors and the registration committee in the local chapter

The quota of one donor for each ten members is only temporary and will be adjusted from time to time as the needs of the various organizations change If it is discovered that a quota of 10 per cent does not provide enough blood to meet the requirements of a particular group, the quota will be increased On the other hand, if there is a comparatively small demand from any group, its quota will be accordingly reduced

MOBILE-UNIT VISITS

The Mobile Unit of the Massachusetts Blood Donor Program will make the following visits during the latter half of January

PLACE	DATE
Chicopee	January 21
Springfield	January 22 and 23
Westfield	January 24

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	January 3	Albert H Brewster
Salem	January 6	Paul W Hugenberger
Haverhill	January 8	William T Green
Brookton	January 9	George W Van Gorder
Gardner (Worcester subclinic)	January 14	John W O'Meara
Pittsfield	January 15	Frank A Slowick
Worcester	January 17	John W O'Meara
Fall River	January 20	David S Grice
Springfield	January 21	Garry deN Hough
Hyannis	January 23	Paul L Norton

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments

MISCELLANY

HUNDREDTH ANNIVERSARY OF A M A

The American Medical Association is going to celebrate its centennial in Atlantic City on June 9-13, 1947, and elaborate plans are being made for this celebration. Only fellows and invited guests are eligible to attend. Membership in a state society is the primary qualification for fellowship in the Association. Fellowship dues and subscription to the *Journal of the American Medical Association* are both included in one annual payment of \$8.00, which is the cost of the periodical to subscribers who are not fellows.

Anyone who is not a fellow and plans to attend the Atlantic City session, which will be a milestone in medical history, can save himself considerable time and confusion when registering, if he will write now to the American Medical Association, 535 North Dearborn Street, Chicago 10, asking if he is eligible to become a fellow.

NOTE

The following appointments to the teaching staff of Harvard Medical School were recently announced: Henry Freeman Allen, of Boston (A B Harvard University 1939, M D Harvard University 1943), fellow in ophthalmic research, Albert Cislér Biegel, of Denver, Colorado (A B University of Colorado 1941, M D Harvard University 1944), fellow in ophthalmic research, David Lukens Coffin, of Boston (V M D University of Pennsylvania School of Veterinary Medicine 1938), research fellow in pathology, Leonard Paul Eliel, of San Francisco, California (S B Harvard University 1936, M D Harvard University 1940), research fellow in pediatrics, Kenneth Austin Evelyn, of Montreal, Canada (S B McGill University 1932, M D, C M McGill University 1938), research associate in medicine, Geoffrey Alan Gilbert, of Birmingham, England (M A Emmanuel College, Cambridge 1939, Ph D Emmanuel College, Cambridge 1943), research fellow in physical chemistry, Avram Goldstein, of New York City (A B Harvard University 1940, M D Harvard University 1943), assistant in pharmacology, John Harold Hanks, of Newton Center (S B Allegheny College 1928, Ph D Yale University 1931), lecturer on bacteriology and immunology, Harper Keith Hellems, of Lewisburg, West Virginia (M D University of Virginia 1943), research fellow in medicine, Elliott Samuel Hurwitt, of Brookville, Pennsylvania (A B Harvard University 1933, M D Harvard University 1937), research fellow in pathology, Robert Kaye, of Philadelphia, Pennsylvania (A B Johns Hopkins University 1939, M D Johns Hopkins University Medical School 1943), assistant in pediatrics, Frederic Koller, of Zurich, Switzerland (A B College of Trogen 1925, M D University of Geneva 1931, Privat-Dozent University of Geneva 1940, associate in medicine, University of Zurich 1944), research fellow in medicine, Evelyn Lenore Oginsky, of Liberty, New York (A B Cornell University 1938, S M University of Chicago 1939, Ph D University of Maryland 1946), research fellow in bacteriology and immunology, Francis Thomas Garnet Prunty, of London, England (M A University of Cambridge 1935, M D University of Cambridge 1944), research

fellow in medicine, Henrik Seyffarth, of Oslo, Norway (M D University of Oslo 1941), research fellow in neurology, William McLean Wallace, of Hyde Park (A B University of Pennsylvania 1934, M D University of Pennsylvania 1938), assistant in pediatrics, Stanley Moore Wyman, of Cambridge (A B Harvard University 1935, M D Harvard University 1939), assistant in radiology, and Leona Zacharias, of Belmont (A B Barnard College 1927, A M Columbia University 1928, Ph D Columbia University 1937), instructor in ophthalmic research.

BOOK REVIEWS

One Hundred Years of Gynaecology, 1800-1900. A comprehensive review of the specialty during its greatest century, with summaries and case reports of all diseases pertaining to women. By James V Ricci, M D. 4th, cloth, 651 pp. Philadelphia: The Blakiston Company, 1945. \$8.50.

This monumental work is a complement, sequel and conclusion to the distinguished author's previously published *Genealogy of Gynaecology*, which summarized the first thirty-eight hundred years of the history of the specialty. The present volume, both a historical document and a reference book, encompasses the gynecologic literature of the nineteenth century, the greatest of its periods. This literature is not merely immense—it is gigantic. The author has accomplished his colossal objective triumphantly and has produced not a bibliographic catalogue but an integrated story of the development of gynecology to its present status. "Dr Ricci's zeal and industry," says Dr Claude Heaton in his introduction, "have crystallized in a work which will for many years to come be the most complete source book on the literature pertinent to the history of gynaecology." The volume concludes with a fragment "Memoirs in Gynaecology" from Dr Henry Clarke Coe, who was to have contributed a chapter on gynecologic trends since 1870.

Fractures and Orthopaedic Surgery for Nurses and Masseurs. By Arthur Naylor, Ch M, M B, M Sc, F R C S (Eng), F R C S (Edin). With a foreword by Ernest Finch, M D, M S (Lond), F R C S (Eng). 8th, cloth, 288 pp., with 243 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$5.00.

Anyone who attempts to write a textbook for nurses finds the task of selection of material most difficult: a little knowledge is a dangerous thing, and for this reason, discussions must not be too detailed but must be complete enough that intelligent nursing care can be given. In this book the author has given a satisfactory exposition of fractures and their treatment; this is the best section of the volume. The chapter on orthopedic apparatus is well written and profusely illustrated. The other sections merely catalogue a number of conditions that the orthopedic surgeon treats. Discussion of these conditions is inadequate for a nursing textbook on orthopedic surgery. This book should be particularly helpful to the nurses assigned to the outpatient or inpatient fracture service of a hospital.

Clinical Traumatic Surgery. By John J Moorhead, M D, D Sc. 8th, cloth, 747 pp., with 500 illustrations. Philadelphia: W B Saunders Company, 1945. \$10.00.

This volume is based on the author's experience of over forty years with the surgery of trauma as medical director of the New York City Transit System and consulting surgeon to numerous New York hospitals. It is written frankly in the first person singular, since "the average reader seeks the opinion of the writer," and therefore contains almost no references to the literature. Safe and simple methods of treatment are emphasized throughout, and the book contains much common sense. The discussion of ruptured intervertebral disk is particularly good. The author's opinion, however, is often considerably at variance with generally accepted standard practice and the experience of others. For example, few surgeons would agree that irrigation of fresh open wounds with alcoholic iodine solution should be recommended as a first-aid measure, or that chromic catgut is satisfactory for closure of the skin after the open reduction of fractures. Nowhere in the chapters on shock

and burns are hematocrit or blood-protein determinations mentioned. For the treatment of contusions the external application of soapsuds is advised and no mention is made of cold and compression. Tracheotomy rather than bronchoscopy is recommended for the removal of foreign bodies from the bronchi. The pages on thrombosis and embolism contain no discussion of heparin, dicoumarol or venous ligation.

Although the book will be of interest to others working in the same field, it cannot be recommended for teaching or as a clinical guide for house officers and residents.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Men Under Stress. By Roy R. Grinker, M.D., and John P. Spiegel, M.D. 8°, cloth, 484 pp. Philadelphia: The Blakiston Company, 1945. \$5.00.

This study on war neuroses is based on the authors' experience in working with combat soldiers overseas in an active theater of operation and with returnees hospitalized for rehabilitation.

The Eternal Ones of the Dream. A psychoanalytic interpretation of Australian myth and ritual. By Géza Róheim, Ph.D. 8°, cloth, 270 pp. New York: International Universities Press, 1945. \$4.50.

Dr Róheim, in this monograph, attempts to apply the most recent developments in psychoanalytic theory to the latest available anthropologic data on the natives of Australia, who are among the most primitive human beings still living in the world. The author investigates the origin of myth, particularly the relation of myth to history and ritual, symbolism and nature mythology. He evolves an entirely new theory on circumcision and discusses extensively the interrelation of dreams, day dreams and historical traditions with myths and rituals.

An Introduction to Medical Science. By William Boyd, M.D., M.R.C.P. (Edin.), F.R.C.P. (Lond.), professor of pathology and bacteriology, University of Toronto. Third edition, thoroughly revised. 8°, cloth, 366 pp., with 125 illustrations. Philadelphia: Lea and Febiger, 1945. \$3.50.

This standard manual for nurses has been revised, and the size has been increased by eight pages. A new chapter has been added on the principles of treatment, dealing with such general matters as rest, the sulfonamides, penicillin, immunotherapy, organotherapy and physiotherapy. New material, including the Rh factor, the relation of sex hormones to cancer of the prostate and disseminated sclerosis, has been added, and the chapter on vitamins has been brought up to date. The newer nomenclature of bacteria has been used. The material is well organized. The book is well printed on good paper, and should prove valuable, not only to nurses but also to other professional medical workers and to medical librarians who have used of a concise manual on medicine.

Studies in Biophysics. The critical temperature of serum (56°C). By Lecomte du Nouÿ, D.Sc., director of the Laboratory of Molecular Serology, University of Paris. 8°, cloth, 185 pp., with 89 illustrations. New York: Reinhold Publishing Corporation, 1945. \$3.50.

This monograph is based on a large amount of experimental work, in which a number of new facts have been brought to light. These facts explain the fundamental problems relating to the mechanism of immunologic reaction and also disclose new problems as yet unsolved. The author has formulated a new hypothesis of a serum molecularly dispersed, comprising albumin, globulins, lipoids and so forth, in a true solution, either in a state of more or less

gradual combinations or free, in contradistinction to the hypothesis of colloidal serum. The author concludes that alexinic activity is a property belonging to the protido-lipoidic complexes, which are molecularly dispersed and which constitute the serum, and not to a separate body. He calls attention to twelve distinct physical phenomena occurring in serum when heated to around 56°C, and concludes that there are profound modifications in the structure of the proteins and of the lipo-protidic complex at around 55 to 56°C. This same temperature brings about the destruction of alexin, and therefore the author concludes that the disappearance of alexin is related to the structural clinical modification determined by heat in a serum molecule as a whole. This monograph should be in all medical-school libraries and reference and bacteriologic collections.

Textbook of Obstetrics. Designed for the use of students and practitioners. By Henricus J. Stander, M.D., professor of obstetrics and gynecology, Cornell University Medical College, obstetrician and gynecologist-in-chief, New York Hospital, and director, Lying-In Hospital, New York City. Stander's third revision. 8°, cloth, 1277 pp., with 739 illustrations. New York: D. Appleton-Century Company, Incorporated, 1945. \$10.00.

This new edition of Dr Stander's textbook, designed for students and practitioners, has been thoroughly revised and brought up to date. This work represents the ninth edition of *Williams Obstetrics*, first published in 1902, but since it embodies the teaching and practice of Dr Stander, the title has been changed. This standard work is recommended for all medical libraries and all physicians practicing obstetrics.

A Textbook of Surgery. Compiled from lectures and other writings of members of the Surgical Department of the Harvard Medical School. By John Homans, M.D. With a special bibliographic index and with 530 illustrations by Willard C. Shepard and others. 8°, cloth, 1278 pp. Springfield, Illinois: Charles C. Thomas, 1945. \$8.00.

This sixth edition of an outstanding work on surgery, first published in 1931, has been thoroughly revised, despite the fact that the text pagination is practically unaltered. Much older and out-of-date material has been deleted and over 188 pages of new material have been added. New surgical developments based on war experience have been incorporated throughout the text. The historical approach to the various surgical subjects has been retained, and a bibliographic, historical index of sixty-eight pages is appended to the text. A comprehensive subject index concludes the volume. This work should be in the collections of all those interested in surgery, as well as in all medical libraries.

Studies from the Rockefeller Institute for Medical Research. Reprints. 4°, paper. Vol 127, 605 pp., 1945. Vol 128, 613 pp., 1946. New York: The Rockefeller Institute for Medical Research.

These two volumes contain the results of investigations conducted in the Rockefeller Institute and elsewhere under its grants and originally published in various serials and here brought together for convenient reference. Each volume has an index of authors and subjects.

The Physiological Basis of Medical Practice. A University of Toronto text in applied physiology. By Charles H. Best, C.B.E., M.A., M.D., D.Sc. (Lond.), F.R.S. and F.R.C.P. (Can.), professor and head, Department of Physiology, and director, Banting-Best Department of Medical Research, University of Toronto, and Norman B. Taylor, V.D., M.D., F.R.S. (Can.), F.R.C.S. (Edin.), F.R.C.P. (Can.), M.R.C.S. (Eng.) and L.R.C.P. (Lond.), professor of physiology, University of Toronto. Fourth edition. 4°, cloth, 1169 pp., with 497 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$10.00.

This fourth edition of a standard textbook is published in a new two-column format that necessitated an entire re-setting of the type. The majority of the illustrations have been reduced to one-column width, and a number of figures have been added and others redrawn. The work has been revised by the addition of new material, and some old mate-

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	January 3	Albert H. Brewster
Salem	January 6	Paul W. Hugenberger
Haverhill	January 8	William T. Green
Brockton	January 9	George W. Van Gorder
Gardner (Worcester subclinic)	January 14	John W. O'Meara
Pittsfield	January 15	Frank A. Slowick
Worcester	January 17	John W. O'Meara
Fall River	January 20	David S. Grice
Springfield	January 21	Garry deN. Hough
Hyannis	January 23	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments

MISCELLANY

HUNDREDTH ANNIVERSARY OF A M A

The American Medical Association is going to celebrate its centennial in Atlantic City on June 9-13, 1947, and elaborate plans are being made for this celebration. Only fellows and invited guests are eligible to attend. Membership in a state society is the primary qualification for fellowship in the Association. Fellowship dues and subscription to the *Journal of the American Medical Association* are both included in one annual payment of \$8.00, which is the cost of the periodical to subscribers who are not fellows.

Anyone who is not a fellow and plans to attend the Atlantic City session, which will be a milestone in medical history, can save himself considerable time and confusion when registering, if he will write now to the American Medical Association, 535 North Dearborn Street, Chicago 10, asking if he is eligible to become a fellow.

NOTE

The following appointments to the teaching staff of Harvard Medical School were recently announced: Henry Freeman Allen, of Boston (A.B. Harvard University 1939, M.D. Harvard University 1943), fellow in ophthalmic research; Albert Cisar Biegel, of Denver, Colorado (A.B. University of Colorado 1941, M.D. Harvard University 1944), fellow in ophthalmic research; David Lukens Coffin, of Boston (V.M.D. University of Pennsylvania School of Veterinary Medicine 1938), research fellow in pathology; Leonard Paul Eliel, of San Francisco, California (S.B. Harvard University 1936, M.D. Harvard University 1940), research fellow in pediatrics; Kenneth Austin Evelyn, of Montreal, Canada (S.B. McGill University 1932, M.D., C.M. McGill University 1938), research associate in medicine; Geoffrey Alan Gilbert, of Birmingham, England (M.A. Emmanuel College, Cambridge 1939, Ph.D. Emmanuel College, Cambridge 1943), research fellow in physical chemistry; Avram Goldstein, of New York City (A.B. Harvard University 1940, M.D. Harvard University 1943), assistant in pharmacology; John Harold Hanks, of Newton Center (S.B. Allegheny College 1928, Ph.D. Yale University 1931), lecturer on bacteriology and immunology; Harper Keith Hellems, of Lewisburg, West Virginia (M.D. University of Virginia 1943), research fellow in medicine; Elliott Samuel Hurwitz, of Brookville, Pennsylvania (A.B. Harvard University 1933, M.D. Harvard University 1937), research fellow in pathology; Robert Kaye, of Philadelphia, Pennsylvania (A.B. Johns Hopkins University 1939, M.D. Johns Hopkins University Medical School 1943), assistant in pediatrics; Frederic Koller, of Zurich, Switzerland (A.B. College of Trogen 1925, M.D. University of Geneva 1931, Privat-Dozent University of Geneva 1940, associate in medicine, University of Zurich 1944), research fellow in medicine; Evelyn Lenore Oginsky, of Liberty, New York (A.B. Cornell University 1938, S.M. University of Chicago 1939, Ph.D. University of Maryland 1946), research fellow in bacteriology and immunology; Francis Thomas Garnet Prunty, of London, England (M.A. University of Cambridge 1935, M.D. University of Cambridge 1944), research

fellow in medicine, Henrik Seyffarth, of Oslo, Norway (M.D. University of Oslo 1941), research fellow in neurology; William McLean Wallace, of Hyde Park (A.B. University of Pennsylvania 1934, M.D. University of Pennsylvania 1938), assistant in pediatrics; Stanley Moore Wyman, of Cambridge (A.B. Harvard University 1935, M.D. Harvard University 1939), assistant in radiology; and Leona Zacharias, of Belmont (A.B. Barnard College 1927, A.M. Columbia University 1928, Ph.D. Columbia University 1937), instructor in ophthalmic research.

BOOK REVIEWS

One Hundred Years of Gynaecology, 1800-1900. A comprehensive review of the specialty during its greatest century, with summaries and case reports of all diseases pertaining to women. By James V. Ricci, M.D. 4°, cloth, 651 pp. Philadelphia: The Blakiston Company, 1945. \$8.50.

This monumental work is a complement, sequel and conclusion to the distinguished author's previously published *Genealogy of Gynaecology*, which summarized the first thirty-eight hundred years of the history of the specialty. The present volume, both a historical document and a reference book, encompasses the gynecologic literature of the nineteenth century, the greatest of its periods. This literature is not merely immense—it is gigantic. The author has accomplished his colossal objective triumphantly and has produced not a bibliographic catalogue but an integrated story of the development of gynecology to its present status. "Dr. Ricci's zeal and industry," says Dr. Claude Heaton in his introduction, "have crystallized in a work which will for many years to come be the most complete source book on the literature pertinent to the history of gynaecology." The volume concludes with a fragment "Memoirs in Gynaecology" from Dr. Henry Clarke Coe, who was to have contributed a chapter on gynecologic trends since 1870.

Fractures and Orthopaedic Surgery for Nurses and Masseuses. By Arthur Naylor, Ch.M., M.B., M.Sc., F.R.C.S. (Eng.), F.R.C.S. (Edin.). With a foreword by Ernest Finch, M.D., M.S. (Lond.), F.R.C.S. (Eng.). 8°, cloth, 288 pp., with 243 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$5.00.

Anyone who attempts to write a textbook for nurses finds the task of selection of material most difficult. A little knowledge is a dangerous thing, and for this reason, discussions must not be too detailed but must be complete enough that intelligent nursing care can be given. In this book the author has given a satisfactory exposition of fractures and their treatment; this is the best section of the volume. The chapter on orthopedic apparatus is well written and profusely illustrated. The other sections merely catalogue a number of conditions that the orthopedic surgeon treats. Discussion of these conditions is inadequate for a nursing textbook on orthopedic surgery. This book should be particularly helpful to the nurses assigned to the outpatient or inpatient fracture service of a hospital.

Clinical Traumatic Surgery. By John J. Moorhead, M.D., D.Sc. 8°, cloth, 747 pp., with 500 illustrations. Philadelphia: W.B. Saunders Company, 1945. \$10.00.

This volume is based on the author's experience of over forty years with the surgery of trauma as medical director of the New York City Transit System and consulting surgeon to numerous New York hospitals. It is written frankly in the first person singular, since "the average reader seeks the opinion of the writer," and therefore contains almost no references to the literature. Safe and simple methods of treatment are emphasized throughout, and the book contains much common sense. The discussion of ruptured intervertebral disk is particularly good. The author's opinion, however, is often considerably at variance with generally accepted standard practice and the experience of others. For example, few surgeons would agree that irrigation of fresh open wounds with alcoholic iodine solution should be recommended as a first-aid measure, or that chromic catgut is satisfactory for closure of the skin after the open reduction of fractures. Nowhere in the chapters on shock

rial has been deleted. Fifty-eight pages of references to the various chapters are appended to the text. A large, comprehensive index concludes the volume. The text is printed in two sizes of type, the smaller of which is rather difficult to read, but is used for less important material. This work should prove valuable to all practicing physicians for reference.

Classic Descriptions of Disease With biographical sketches of the authors. By Ralph H. Major, M.D., professor of medicine, University of Kansas School of Medicine. Third edition. 4°, cloth, 679 pp., with 158 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$6.50.

This third edition of a standard work in the field of the history of medicine, first published in 1932, has been revised by the addition of several new selections, and a bibliography has been added for the first time. Dr. Major has made two hundred and eighty-seven selections from the original accounts of one hundred and ninety-five physicians of all countries whose contributions and discoveries in the field of clinical medicine have been outstanding. These accounts are either the first known, one of the earliest or one of the most interesting accounts in question. The whole field of clinical medicine is covered from the time of the Papyrus Ebers, one thousand years before Hippocrates, to modern times. The work is divided into ten subject sections which are preceded by a historical summary and often by short biographic sketches. The original accounts have been translated into English wherever necessary, and the text is illustrated with carefully chosen portraits and facsimiles of titles and texts and drawings of apparatus. The book should be in all medical libraries, as well as in the collections of physicians interested in the history of medicine.

Psychiatry in Modern Warfare. By Edward A. Strecker, M.D., Litt D., LL.D., professor of psychiatry and chairman of the department, University of Pennsylvania School of Medicine, and Kenneth E. Appel, Ph.D., M.D., Sc.D., assistant professor of psychiatry and chief of clinic, University of Pennsylvania School of Medicine, and lecturer in psychiatry, School of Neuropsychiatry, United States Naval Hospital, Philadelphia. 12°, cloth, 88 pp. New York: The Macmillan Company, 1945. \$1.50.

The modern aspects of psychiatry as applied to the disasters associated with war are reviewed. The text is sound, and the book can be recommended. Although brief, it contains much that is pertinent to present conditions.

Diseases of the Nervous System. By F. M. R. Walshe, O.B.E., M.D., D.Sc., F.R.C.P. (Lond.), D.Sc. (hon.), physician in charge of the Neurological Department, University College Hospital, London, physician to the National Hospital for Nervous Diseases, Queen Square, neurologist to the Hospital for Tropical Diseases, London, and to the Seamen's Hospital, Greenwich, and fellow of University College, London. Fourth edition. 8°, cloth, 360 pp., with 51 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$4.50.

This popular small book, designed for practitioners and students, has passed into its fourth edition during the war years, a tribute to the soundness of the author's contribution. Some new material has been added, but in general the book remains as it was when first issued—a sound résumé of the subject, with emphasis on the clinical aspects of neurology. The author has been reasonably successful in keeping the book up to date, but the task is not an easy one and some modern advances are not given full recognition. Conservatism, however, is the keynote of the book and perhaps its most valuable asset. This volume, as a brief text of value to the clinician, can be given unqualified approval.

Take It Easy. The art of conquering your nerves. By Arthur G. Mathews. 8°, cloth, 239 pp., with 26 symbolical illustrations. New York: Sheridan House, 1945. \$2.98.

The author has attempted to express in lay terms the present conception of neuroses and their treatment. In addition to the text he has used simple diagrams. In general his book is sound, but oversimplification detracts from its value. It is not a book that should receive unqualified recommendation.

NOTICES

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Friday, January 3 — Pulmonary Disease in Modern Industry
Dr. Harriet Hardy

Wednesday, January 8 — Motion Picture: Energy Release from Food

Friday, January 10 — Sterility. Dr. Somers Sturgis

Wednesday, January 15 — Rheumatic Fever. Dr. T. Duckett Jones

Friday, January 17 — Changes in Biologicals and in Human Reactions. Dr. Ralph E. Wheeler

Wednesday, January 22 — Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon

Friday, January 24 — Parenteral Fluid Therapy for the Starving Dehydrated Patient, Infant and Adult. Dr. Allan Butler

Wednesday, January 29 — Nasal Resistance Inhaler: A new method for the prevention and treatment of aerotitis media and aerotitis sinusitis. Dr. H. F. Sternstein

Friday, January 31 — Gout. Dr. Elmer C. Bartels

On Tuesday and Thursday mornings, Dr. S. J. Thibaut will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek. Medical rounds are conducted each weekday except Saturdays by members of the staff from 12:00 to 1:00 in the Lecture Hall.

All exercises are open to the medical profession.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, January 7, at 8:15 p.m. Dr. Leo M. Davidoff, of the Montefiore Hospital, New York City, will talk on "Recent Advances in Brain Surgery."

NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, January 2, at 7:15 p.m., in the classroom of the Nurses' Residence. Dr. Edward L. Young will speak on "Gall Bladder Disease Associated with Duodenal Ulcer and Hypertension." Dr. Dorothy K. Scheidell will be chairman.

NATIONAL CONFERENCE ON MEDICAL SERVICE

The twentieth annual meeting of the National Conference on Medical Service will be held at the Palmer House, Chicago, Illinois, on February 9. Registration will commence at 9:00 a.m., and the program will include discussions in the fields of national affairs, economics and medical education. All physicians are invited to attend; there is no registration fee. Dr. Cleon A. Nafe, of Indianapolis, is president of the conference, and Dr. Creighton Barker, of New Haven, Connecticut, is secretary.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JANUARY 2

THURSDAY, JANUARY 2
7:15 p.m. Monthly Clinical Conference and Meeting of the Staff Nurses' Residence, New England Hospital for Women and Children

FRIDAY, JANUARY 3
9:00-10:00 a.m. Pulmonary Disease in Modern Industry. Dr. Harriet Hardy. Joseph H. Pratt Diagnostic Hospital

MONDAY, JANUARY 6
12:15-1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital

(Notices continued on page xxi)

